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     FILE 'USPATFULL, CAPLUS' ENTERED AT 09:46:31 ON 13 AUG 2002
L1          8457 FILE USPATFULL
L2         15706 FILE CAPLUS
     TOTAL FOR ALL FILES
L3         24163 S ASPIRIN

     FILE 'REGISTRY' ENTERED AT 09:46:42 ON 13 AUG 2002
L4             1 S ASPIRIN/CN

     FILE 'USPATFULL, CAPLUS' ENTERED AT 09:47:18 ON 13 AUG 2002
L5          9939 FILE USPATFULL
L6         23400 FILE CAPLUS
     TOTAL FOR ALL FILES
L7         33339 S L4 OR ASPIRIN OR (ACETYLSALICYLIC ACID)
L8           352 FILE USPATFULL
L9            57 FILE CAPLUS
     TOTAL FOR ALL FILES
L10          409 S L7 AND (FACTOR XA)
L11          146 FILE USPATFULL
L12            2 FILE CAPLUS
     TOTAL FOR ALL FILES
L13          148 S L10 AND SYNERG?
L14           37 FILE USPATFULL
L15           68 FILE CAPLUS
     TOTAL FOR ALL FILES
L16          105 S ENOXAPARIN AND (FACTOR XA)
L17            8 FILE USPATFULL
L18           45 FILE CAPLUS
     TOTAL FOR ALL FILES
L19           53 S ENOXAPARIN (1S) (FACTOR XA)

     FILE 'CAPLUS' ENTERED AT 09:52:59 ON 13 AUG 2002
                E FACTOR XA/CT
                E E3+ALL
L20             0 S E13 AND E14
L21          3145 S E13 OR E14
                E E14+ALL
L22          3039 S (E16-E20) AND XA
L23             2 S L22 AND L7 AND SYNERG?
L24             0 S 9002-05-5/RL
L25          2482 S 9002-05-5/BIOL
L26            17 S L25 AND ASPIRIN
L27            34 S L25 AND L7
L28            29 S L27 AND XA
L29             2 S L28 AND (SYNERG? OR SUBTHERAPEUTIC?)

     FILE 'USPATFULL, PCTFULL, EUROPATFULL' ENTERED AT 10:08:44 ON 13 AUG 2002
L30          1129 FILE USPATFULL
L31             0 FILE PCTFULL
L32             0 FILE EUROPATFULL
     TOTAL FOR ALL FILES
L33          1129 S L4

=> s l7
L34          9939 FILE USPATFULL
'CN' IS NOT A VALID FIELD CODE
L35           426 FILE PCTFULL
'CN' IS NOT A VALID FIELD CODE
L36          1972 FILE EUROPATFULL

TOTAL FOR ALL FILES
L37         12337 L7
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280772-94-3P 280772-95-4P 280772-96-5P 280772-97-6P 280772-98-7P
280772-99-8P 280773-00-4P 280773-01-5P 280773-02-6P 280773-03-7P
280773-04-8P 280773-05-9P 280773-06-0P 280773-08-2P 280773-09-3P
280773-10-6P 280773-11-7P 280773-12-8P 280773-13-9P 280773-15-1P
280773-16-2P 280773-17-3P 280773-18-4P 280773-20-8P 280773-21-9P
280773-22-0P 280773-24-2P 280773-25-3P 280773-26-4P 280773-27-5P
280773-28-6P 280773-30-0P 280773-31-1P 280773-32-2P 280773-34-4P
280773-35-5P 280773-36-6P 280773-37-7P 280773-40-2P 280773-42-4P
280773-43-5P 280773-44-6P 280773-46-8P 280773-47-9P 280773-48-0P
280773-49-1P 280773-50-4P 280773-52-6P 280773-53-7P 280773-54-8P
280773-55-9P 280773-57-1P 280773-58-2P 280773-60-6P 280773-61-7P
280773-63-9P 280773-64-0P 280773-66-2P 280773-67-3P 280773-68-4P
280773-69-5P 280773-70-8P 280773-72-0P 280773-73-1P 280773-75-3P
280773-76-4P 280773-78-6P 280773-79-7P 280773-81-1P 280773-82-2P
280773-84-4P 280773-85-5P 280773-86-6P 280773-87-7P 280773-89-9P
280773-90-2P 280773-91-3P 280773-93-5P 280773-94-6P 280773-96-8P
280773-97-9P 280773-98-0P 280773-99-1P 280774-00-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 280774-01-8P 280774-02-9P 280774-03-0P 280774-04-1P 280774-05-2P
280774-06-3P 280774-07-4P 280774-08-5P 280774-09-6P 280774-15-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Beight Douglas Wade; WO 9900121 A 1999 CAPLUS
(2) Beight Douglas Wade; WO 9900128 A 1999 CAPLUS
(3) Berlex Lab; WO 9628427 A 1996 CAPLUS
(4) Katakura; EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY CHIMICA THERAPEUTICA 1995, V30(5), P387 CAPLUS
(5) Kunitada, S; CURRENT PHARMACEUTICAL DESIGN 1996, V2(5), P6
(6) Schering Ag; WO 9932477 A 1999 CAPLUS

L28 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:116927 CAPLUS
DN 132:150612
TI Use of anti-coagulation factor antibodies as long-lasting protective agents
IN Feuerstein, Giora Zeev
PA Smithkline Beecham Corp., USA
SO PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-395
CC 15-3 (Immunochemistry)
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000007626 | A1 | 20000217 | WO 1999-US17704 | 19990803 |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| US 2001018052 | A1 | ~~20010830~~ | US 2001-817960 | 20010327 |
| PRAI US 1998-95714P | P | 19980807 | | |
| US 1999-359202 | B1 | 19990722 | | |

AB The use of antibodies and antigen-binding fragments directed against coagulation factors and their use in inhibiting thrombosis are disclosed.

ST monoclonal antibody blood coagulation factor thrombosis

IT Heart, disease
(angina pectoris, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Drugs
(anti-platelet; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Blood vessel
(artificial, thrombosis assocd. with shunts; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Organ, animal
(artificial, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Heart, disease
(atrial fibrillation, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Artery
(coronary, angioplasty, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Blood coagulation
(disseminated intravascular, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Lung, disease
(embolism, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Heart, disease
(infarction, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(monoclonal; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Brain, disease
(stroke, thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Kidney, disease
Prosthetic materials and Prosthetics
(thrombosis assocd. with; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Animal
Platelet (blood)
Sepsis
Thrombosis
(use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Antibodies
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Blood-coagulation factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of anti-coagulation factor antibodies as long-lasting protective agents)
IT Thrombosis
(venous, deep; use of anti-coagulation factor antibodies as long-lasting protective agents)
IT 9001-24-5, Blood coagulation factor V 9001-25-6, Blood coagulation factor VII 9001-27-8, Blood coagulation factor VIII 9001-28-9, Blood coagulation factor IX 9001-29-0, Blood coagulation factor X 9002-04-4, Thrombin **9002-05-5**, Blood coagulation factor **Xa**
9013-55-2, Blood coagulation factor XI 37203-61-5, Blood coagulation factor XIa 37316-87-3, Blood coagulation factor IXa 65312-43-8, Blood

**Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

TI Inhibitors of factor Xa with a neutral P1 specificity group
AN 1999:160040 USPATFULL
PI US 5998424 19991207

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L10 ANSWER 19 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI .alpha.-branched anilines, toluenes, and analogs thereof as factor Xa inhibitors
AN 1999:99692 USPATFULL
PI US 5942544 19990824

L10 ANSWER 20 OF 24 USPATFULL
DETD Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other Factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI Isoxazoline, isothiazoline and pyrazoline factor Xa inhibitors
AN 1999:96369 USPATFULL
PI US 5939418 19990817

L10 ANSWER 21 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI N-(amidinophenyl) cyclourea analogs as factor XA inhibitors
AN 1999:81827 USPATFULL
PI US 5925635 19990720

L10 ANSWER 22 OF 24 USPATFULL
SUMM The compositions and methods of the present invention comprising fibrinogen receptor antagonists are useful in **combination** with procedures for treating patients with other anticoagulants (e.g. thrombin inhibitors such as **heparin** and Factor **Xa inhibitors** such as **warfarin**), thrombolytic agents (e.g. streptokinase and tissue plasminogen activator), and platelet antiaggregation agents (e.g. **aspirin** and dipyridamole).
TI Methods for administering integrin receptor antagonists
AN 1999:53625 USPATFULL
PI US 5900414 19990504

L10 ANSWER 23 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the

publications identified above under Background of the Invention.
TI Amidinoindoles, amidinoazoles, and analogs thereof
AN 1999:37302 USPATFULL
PI US 5886191 19990323

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L10 ANSWER 24 OF 24 USPATFULL
DETD These compounds may be used alone or in **combination** with other diagnostic, anticoagulant, antiplatelet or fibrinolytic agents. For example adjunctive administration of factor **Xa** **inhibitors** with standard **heparin**, low molecular weight **heparin**, direct thrombin inhibitors (i.e. hirudin), **aspirin**, fibrinogen receptor antagonists, streptokinase, urokinase and/or tissue plasminogen activator may result in greater antithrombotic or thrombolytic efficacy or efficiency. The. . .
TI Substituted (sulfinic acid, sulfonic acid, sulfonylamino or sulfinylamino) N-[(aminoiminomethyl)phenylalkyl]-azaheterocyclylamide compounds
AN 97:22796 USPATFULL
PI US 5612353 19970318

=> d 1 ibib

L10 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:645898 CAPLUS
DOCUMENT NUMBER: 133:232835
TITLE: Treatment of thrombosis by combined use of a factor xa inhibitor and aspirin, tissue plasminogen activator (TPA), a GPIIb/IIIa antagonist, low molecular weight heparin or heparin
INVENTOR(S): Wong, Pancras C.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000053264 | A1 | 20000914 | WO 2000-US6451 | 20000310 |

W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: US 1999-123815 P 19990311
REFERENCE COUNT: 10
REFERENCE(S):
(1) Boehringer Ingelheim Pharma; DE 19816983 A 1999 CAPLUS
(2) Cor Therapeutics Inc; WO 9640744 A 1996 CAPLUS
(3) Du Pont Merck Pharma; WO 9514683 A 1995 CAPLUS
(4) Du Pont Merck Pharma; WO 9828269 A 1998 CAPLUS
(5) Hamilton Civic Hospitals Res; EP 0735050 A 1996 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=>

L10 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2001 ACS
IT 9002-05-5, Factor **xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antithrombotic formulation **combining** **aspirin** with an anti-Xa oligosaccharide)
TI Antithrombotic formulation combining aspirin with an anti-Xa oligosaccharide
AN 1999:458944 CAPLUS
DN 131:78465

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |
| AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| AU 9716319 | A1 | 19980917 | | |

L10 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2001 ACS
IT 9002-05-5, Coagulation factor **Xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antithrombotics contg. **aspirin** and an anti-Xa oligosaccharide and use of anti-Xa oligosaccharides in **combination** with **aspirin**)
TI Compositions containing an association of aspirin and an anti-Xa oligosaccharide and use of anti-Xa oligosaccharide optionally in combination with aspirin
AN 1999:401026 CAPLUS
DN 131:35871

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| AU 9716319 | A1 | 19980917 | | |
| BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |

L11 ANSWER 7 OF 17 USPATFULL
SUMM . . . inhibit HIV infection or treat the symptoms of HIV infection in
a host. The combination of compounds is preferably a **synergistic** combination. Synergy, as described for example by Chou and Talalay, Adv.
Enzyme Regul. 22:27-55 (1984), occurs when the effect (in. . . combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a **synergistic** effect is most clearly demonstrated at suboptimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased. . .
DETD . . . Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
DETD . . . may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or **synergistic** effect of the therapeutic agents when administered in combination.

ACCESSION NUMBER: 2000:57785 USPATFULL
TITLE: 6-membered aromatics as factor Xa inhibitors
INVENTOR(S): Pruitt, James Russell, Landenberg, PA, United States
Pinto, Donald Joseph Phillip, Newark, DE, United States
Quan, Mimi Lifen, Newark, DE, United States
Wexler, Ruth Richmond, Wilmington, DE, United States
PATENT ASSIGNEE(S): Dupont Pharmaceuticals, Wilmington, DE, United States (U.S. corporation)

L11 ANSWER 6 OF 17 USPATFULL

SUMM . . . Sci. USA 84:6899-6903, 1987), and this amplification is correlated with poor patient prognosis. Simultaneous overexpression of p185.sup.neu and the EGFR **synergistically** transforms rodent fibroblasts and this condition is often observed in human cancers. Finally, HER3 expression is amplified in a variety. . .

DETD . . . thrombin inhibitors can be co-administered with suitable anti-coagulation agents or thrombolytic agents such as plasminogen activators or streptokinase to achieve **synergistic** effects in the treatment of various vascular pathologies. For example, thrombin inhibitors enhance the efficiency of tissue plasminogen activator-mediated thrombolytic. . .

DETD . . . they are useful for the isolation of mammalian serum from the blood they may alternatively contain clot-inhibiting additives (such as **heparin** salts, EDTA salts, citrate salts or oxalate salts), in which case, they are useful for the isolation of mammalian plasma from the blood. The compounds of the present invention are potent **inhibitors** of factor **Xa** or thrombin, and as such, can be incorporated into blood collection tubes to prevent clotting of the mammalian blood drawn. . .

ACCESSION NUMBER: 2000:121539 USPATFULL
TITLE: Methods for regulating transcription factors
INVENTOR(S): Qabar, Maher N., Redmond, WA, United States
McMillan, Michael K., Bellevue, WA, United States
Kahn, Michael S., Kirkland, WA, United States
Tulinsky, John E., Seattle, WA, United States
Ogbu, Cyprian O., Bellevue, WA, United States
Mathew, Jessymol, Bellevue, WA, United States
PATENT ASSIGNEE(S): Molecumetics Ltd., Bellevue, WA, United States (U.S. corporation)

| | NUMBER | DATE |
|---|---|---|
| PATENT INFORMATION: | US 6117896 | 20000912 |
| APPLICATION INFO.: | US 1998-22934 | 19980212 (9) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 1997-797915, filed on 10 Feb 1997, now abandoned And a continuation-in-part of Ser. No. US 692420 | |
| PRIORITY INFORMATION: | US 1997-47067 | 19970519 (60) |

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Higel, Floyd D.
LEGAL REPRESENTATIVE: Seed Intellectual Property Law Group PLLC
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Figure(s); 6 Drawing Page(s)
LINE COUNT: 4501
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 5 OF 17 USPATFULL

SUMM . . . be administered in combination with one or more additional therapeutic agents selected from: anti-coagulant or coagulation inhibitory agents, such as **heparin** or **warfarin**; anti-platelet or platelet inhibitory agents, such as **aspirin**, piroxicam, ticlopidine, or clopidogrel; factor **Xa** **inhibitors**; thrombin **inhibitors** such as boropeptides, hirudin or argatroban; or thrombolytic or fibrinolytic agents, such as plasminogen activators, anistreplase, urokinase, or streptokinase.

SUMM . . . margin of safety for each component when used as a single agent. Such combination therapies may be employed to achieve **synergistic** or additive therapeutic effects for the treatment of thromboembolic disorders.

DETD . . . may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or **synergistic** effect which would be obtained as a result of addition of further agents in accordance with the present invention.

ACCESSION NUMBER: 2000:134898 USPATFULL
TITLE: Integrin receptor antagonists
INVENTOR(S): Wityak, John, West Grove, PA, United States
Tobin, Aleksandra Ewa, Lincoln University, PA, United States
PATENT ASSIGNEE(S): DuPont Pharmaceuticals, Wilmington, DE, United States (U.S. corporation)

| | NUMBER | DATE | |
|---|---|---|---|
| PATENT INFORMATION: | US 6130231 | 20001010 | |
| APPLICATION INFO.: | US 1997-980016 | 19971126 | (8) |

| | NUMBER | DATE |
|---|---|---|

L11 ANSWER 7 OF 17 USPATFULL
SUMM . . . inhibit HIV infection or treat the symptoms of HIV infection in
a host. The combination of compounds is preferably a **synergistic** combination. Synergy, as described for example by Chou and Talalay, Adv.
Enzyme Regul. 22:27-55 (1984), occurs when the effect (in. . . . combination is greater than the additive effect of the compounds when administered alone as a single agent. In general, a **synergistic** effect is most clearly demonstrated at suboptimal concentrations of the compounds. Synergy can be in terms of lower cytotoxicity, increased. . .

DETD . . . Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

DETD . . . may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or **synergistic** effect of the therapeutic agents when administered in combination.

ACCESSION NUMBER: 2000:57785 USPATFULL
TITLE: 6-membered aromatics as factor Xa inhibitors
INVENTOR(S): Pruitt, James Russell, Landenberg, PA, United States
Pinto, Donald Joseph Phillip, Newark, DE, United States
Quan, Mimi Lifen, Newark, DE, United States
Wexler, Ruth Richmond, Wilmington, DE, United States
PATENT ASSIGNEE(S): Dupont Pharmaceuticals, Wilmington, DE, United States (U.S. corporation)

| | NUMBER | DATE | |
|---|---|---|---|
| PATENT INFORMATION: | US 6060491 | 20000509 | |
| APPLICATION INFO.: | US 1998-99663 | 19980618 | (9) |

L11 ANSWER 11 OF 17 USPATFULL

DETD . . . thrombin inhibitors can be co-administered with suitable anti-coagulation agents or thrombolytic agents such as plasminogen activators or streptokinase to achieve **synergistic** effects in the treatment of various ascular pathologies. For example, thrombin inhibitors enhance the efficiency of tissue plasminogen activator-mediated thrombolytic. . .

DETD . . . they are useful for the isolation of mammalian serum from the blood they may alternatively contain clot-inhibiting additives (such as **heparin** salts, EDTA salts, citrate salts or oxalate salts), in which case, they are useful for the isolation of mammalian plasma from the blood. The compounds of the present invention are potent **inhibitors** of factor **Xa** or thrombin, and as such, can be incorporated into blood collection tubes to prevent clotting of the mammalian blood drawn. . .

ACCESSION NUMBER: 2000:12794 USPATFULL

TITLE: .beta.-sheet mimetics and use thereof as protease inhibitors

INVENTOR(S): Kahn, Michael, Kirkland, WA, United States

PATENT ASSIGNEE(S): Molecumetics, Ltd., Bellevue, WA, United States (U.S. corporation)

| | NUMBER | DATE |
|---|---|---|
| PATENT INFORMATION: | US 6020331 | 20000201 |
| APPLICATION INFO.: | US 1998-9386 | 19980120 (9) |

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-624695, filed on 25 Mar 1996, now abandoned which is a continuation-in-part of Ser. No. US 1995-549006, filed on 27 Oct 1995, now abandoned which is a continuation-in-part of Ser. No. US 1995-410518, filed on 24 Mar 1995, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Woodward,

L11 ANSWER 16 OF 17 USPATFULL

DETD . . . Other anticoagulant agents (or coagulation inhibitory agents) that may be used in combination with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

DETD . . . may be reduced relative to the usual dosage of the agent when administered alone, in view of the additive or **synergistic** effect of the therapeutic agents when administered in combination.

ACCESSION NUMBER: 1999:37302 USPATFULL
TITLE: Amidinoindoles, amidinoazoles, and analogs thereof
INVENTOR(S): Dominguez, Celia, Newark, DE, United States
Han, Qi, Wilmington, DE, United States
Duffy, Daniel Emmett, Wilmington, DE, United States
Park, Jeongsook Maria, Bear, DE, United States
Quan, Mimi Lifen, Newark, DE, United States
Rossi, Karen Anita, Wilmington, DE, United States
Wexler, Ruth Richmond, Wilmington, DE, United States
PATENT ASSIGNEE(S): DuPont Pharmaceuticals Company, Wilmington, DE, United States (U.S. corporation)

| | NUMBER | DATE | |
|---|---|---|---|
| PATENT INFORMATION: | US 5886191 | 19990323 | |
| APPLICATION INFO.: | US 1997-916736 | 19970818 | (8) |
| DOCUMENT TYPE: | Utility | | |
| PRIMARY EXAMINER: | Richter, Johann | | |
| ASSISTANT EXAMINER: | Keating, Dominic | | |
| LEGAL REPRESENTATIVE: | Vance, David H. | | |
| NUMBER OF CLAIMS: | 8 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 4385 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 17 OF 17 USPATFULL

SUMM . . . aspect of the invention there is provided a diagnostic kit for determining anti-coagulant activity of heparin in a sample, comprising **synergistic** amounts of:

DETD . . . the present invention are based on purified coagulation factors, such as thrombin or Factor Xa, in competing reactions between a **heparin** dependent irreversible inhibitor such as a protease and more specifically antithrombin III or **heparin** cofactor II plus **heparin** and a **heparin**-independent irreversible inhibitor for the enzyme such as highly specific peptidyl chloromethyl ketone **inhibitors** of Factor **Xa** or thrombin, or chromogenic or fluorescent substrates of the two enzymes. Peptidyl para-nitroanilide chromogenic substrate is a preferred substrate. The. . .

DETD . . . It is contemplated that a diagnostic kit for use in a routine blood testing laboratory or the like would comprise **synergistic** amounts of: a selected coagulation enzyme, generally selected from thrombin and Factor Xa; and irreversible heparin dependent protease inhibitor, such. . .

| | | | |
|---|---|---|---|
| ACCESSION NUMBER: | 94:37852 USPATFULL | | |
| TITLE: | Method for measuring heparin | | |
| INVENTOR(S): | Nesheim, Michael E., Kingston, Canada<br>Manuel, Reginald P., Sydenham, Canada | | |
| PATENT ASSIGNEE(S): | Research Corporation Technologies, Inc., Tucson, AZ, United States (U.S. corporation) | | |
| | NUMBER | DATE | |
| PATENT INFORMATION: | US 5308755 | 19940503 | |
| APPLICATION INFO.: | US 1992-895078 | 19920608 | (7) |
| DOCUMENT TYPE: | Utility | | |
| PRIMARY EXAMINER: | Kepplinger, Esther L. | | |
| ASSISTANT EXAMINER: | Green, Lora M. | | |
| LEGAL REPRESENTATIVE: | Scully, Scott, Murphy & Presser | | |
| NUMBER OF CLAIMS: | 4 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 8 Drawing Figure(s); 4 Drawing Page(s) | | |
| LINE COUNT: | 385 | | |

L10 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2001 ACS
IT 9002-05-5, Factor **xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antithrombotic formulation **combining** **aspirin** with an anti-Xa oligosaccharide)
TI Antithrombotic formulation combining aspirin with an anti-Xa oligosaccharide
AN 1999:458944 CAPLUS
DN 131:78465

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |
| AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| AU 9716319 | A1 | 19980917 | | |

L10 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2001 ACS
IT 9002-05-5, Coagulation factor **Xa**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**inhibitors**; antithrombotics contg. **aspirin** and an anti-Xa oligosaccharide and use of anti-Xa oligosaccharides in **combination** with **aspirin**)
TI Compositions containing an association of aspirin and an anti-Xa oligosaccharide and use of anti-Xa oligosaccharide optionally in combination with aspirin
AN 1999:401026 CAPLUS
DN 131:35871

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| AU 9716319 | A1 | 19980917 | | |
| BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |

L10 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2001 ACS
AB . . . therapy, addnl. administration of vWF, either simultaneously or subsequently, decreases the risk of bleeding. Anticoagulants with which vWF may be **combined** include **heparin** and its derivs.; synthetic low-mol.-wt. thrombin inhibitors; synthetic or recombinant factor **Xa** or factor VII **inhibitors**; blood platelet antagonists or antibodies; and vitamin K antagonists. Fibrinolytics which may be used with vWF include streptokinase, plasminogen activators, . .
TI Therapeutic combination of von Willebrand factor (vWF) with antithrombotics and fibrinolytics
AN 1996:307743 CAPLUS
DN 124:333088

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI DE 4437544 | A1 | 19960425 | DE 1994-4437544 | 19941020 |
| EP 713881 | A2 | 19960529 | EP 1995-114846 | 19950921 |
| EP 713881 | A3 | 19960821 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| FI 9504964 | A | 19960421 | FI 1995-4964 | 19951018 |
| AU 9534304 | A1 | 19960502 | AU 1995-34304 | 19951018 |
| AU 708670 | B2 | 19990812 | | |
| CN 1128168 | A | 19960807 | CN 1995-118715 | 19951018 |
| US 5571784 | A | 19961105 | US 1995-544867 | 19951018 |
| CA 2160975 | AA | 19960421 | CA 1995-2160975 | 19951019 |
| NO 9504175 | A | 19960422 | NO 1995-4175 | 19951019 |

| | | | | |
|---|---|---|---|---|
| ZA 9508838 | A | 19960513 | ZA 1995-8838 | 19951019 |
| JP 08208504 | A2 | 19960813 | JP 1995-270785 | 19951019 |
| HU 73762 | A2 | 19960930 | HU 1995-3031 | 19951020 |

L10 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2001 ACS

AB . . . of a series of bovine pancreatic trypsin inhibitor mutants (BPTI, aprotinin) 4C2, 7L22, 5L15, 5L15-PEG, 6L15 and 5L84 with a **combined inhibitory** activity on factor **Xa**, factor VIIa-tissue factor complex, factor XIa and plasma kallikrein were compared to rTAP, r-hirudin, **heparin** and enoxaparin in a platelet rich thrombosis model in hamsters. Platelet dependent thrombus deposition was quantified by dedicated image anal.. . .

TI Characterization of a novel series of aprotinin-derived anticoagulants. II. Comparative antithrombotic effects on primary thrombus formation in vivo

AN 1995:796978 CAPLUS

DN 123:246407

L10 ANSWER 6 OF 24 USPATFULL

DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

TI Benzimidazolinones, benzoxazolinones, benzopiperazinones, indanones, and derivatives thereof as inhibitors of factor Xa

AN 2001:44255 USPATFULL

PI US 6207697 20010327

L10 ANSWER 7 OF 24 USPATFULL

DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

TI Disubstituted pyrazolines and triazolines as factor Xa inhibitors

AN 2001:25924 USPATFULL

PI US 6191159 20010220

L10 ANSWER 8 OF 24 USPATFULL

DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.

TI Phenyl-isoxazoles as factor XA Inhibitors

AN 2001:22243 USPATFULL

PI US 6187797 20010213

L10 ANSWER 9 OF 24 USPATFULL

DETD These compounds may be used alone or in **combination** with other diagnostic, anticoagulant, antiplatelet or fibrinolytic agents. For

antithrombotic or thrombolytic efficacy or efficiency. The. . .
TI Substituted n-[(aminoiminomethyl or aminomethyl)phenyl]propyl amides
AN 2000:80775 USPATFULL
PI US 6080767 20000627

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L10 ANSWER 14 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI 6-membered aromatics as factor Xa inhibitors
AN 2000:57785 USPATFULL
PI US 6060491 20000509

L10 ANSWER 15 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI Amidinophenyl-pyrrolidines, -pyrrolines, and -isoxazolidines and derivatives thereof
AN 2000:54125 USPATFULL
PI US 6057342 20000502

L10 ANSWER 16 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI Amidinoindoles, amidinoazoles, and analogs thereof
AN 2000:37813 USPATFULL
PI US 6043257 20000328

L10 ANSWER 17 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor **Xa inhibitors** such as those described in the publications identified above under Background of the Invention.
TI Nitrogen containing heteroaromatics as factor Xa inhibitors
AN 2000:12820 USPATFULL
PI US 6020357 20000201

L10 ANSWER 18 OF 24 USPATFULL
DETD . . . so as to provide the desired therapeutic effect. Other anticoagulant agents (or coagulation inhibitory agents) that may be used in **combination** with the compounds of this invention include **warfarin** and **heparin**, as well as other factor

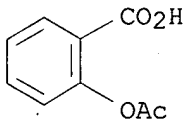
L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2002 ACS
RN 50-78-2 REGISTRY
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-(Acetyloxy)benzoic acid
CN 2-Acetoxybenzoic acid
CN 2-Carboxyphenyl acetate
CN A.S.A. Empirin
CN AC 5230
CN Acenterine
CN Acesal
CN Acesan
CN Acetard
CN Aceticyl
CN Acetilum acidulatum
CN Acetisal
CN Acetol
CN Acetophen
CN Acetosal
CN Acetosalic acid
CN Acetosalin
CN Acetylin
CN Acetylsal
CN Acetylsalicylic acid
CN Acetysal
CN Acidum acetylsalicylicum
CN Acisal
CN Acylpyrin
CN ASA
CN Asagran
CN **Aspirin**
CN Aspirin Protect 100
CN Aspirin Protect 300
CN Aspirina 03
CN Aspro
CN Aspro Clear
CN Aspropharm
CN Asteric
CN Benaspir
CN Bialpirina
CN Caprin
CN Colfarit
CN Dolean pH 8
CN Doril
CN Duramax
CN ECM
CN Ecotrin
CN Empirin
CN Endosprin
CN Endydol
CN Enterosarine
CN Entrophen
CN Globentyl
CN Globoid
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD
DR 11126-35-5, 11126-37-7, 98201-60-6, 2349-94-2, 26914-13-6
MF C9 H8 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,

BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HODOC*, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PHARMASEARCH, PIRA, PROMT, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB

(*File contains numerically searchable property data)

Other Sources: DSL**, EINECS**, TSCA**

(**Enter CHEMLIST File for up-to-date regulatory information)




**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

14341 REFERENCES IN FILE CA (1967 TO DATE)
282 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
14361 REFERENCES IN FILE CAPLUS (1967 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=>

L12 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
AN 1993:485705 CAPLUS
DN 119:85705
TI Comparative effects of enoxaparin and heparin on arterial and venous clot lysis with alteplase in dogs
AU Stassen, Jean Marie; Rapold, Hans J.; Vanlinthout, Ingrid; Collen, Desire
CS Cent. Thromb. Vasc. Res., Univ. Leuven, Louvain, B-3000, Belg.
SO Thromb. Haemostasis (1993), 69(5), 454-9
CODEN: THHADQ; ISSN: 0340-6245
DT Journal
LA English
CC 1-8 (Pharmacology)
AB The effects of enoxaparin and heparin on arterial and venous thrombolysis induced with alteplase (Actilyse) were compared in a randomized blind study in dogs pretreated with **aspirin**. The dogs were pretreated with **aspirin** because it is widely used in assocn. with thrombolysis in patients with acute myocardial infarction. Enoxaparin and heparin were equipotent in terms of the arterial patency time when the dose was expressed in anti-Xa activity. When the dose of anticoagulant was expressed in anti-IIa, enoxaparin was significantly more potent than heparin. Conversely, with respect to venous clot lysis, enoxaparin was equipotent to heparin on the basis of their anti-IIa activity, but heparin was more potent than enoxaparin on the basis of their anti-Xa activity.
ST alteplase blood clot lysis enoxaparin heparin
IT Anticoagulants and Antithrombotics
(enoxaparin and heparin, alteplase thrombolysis enhancement by, comparison of)
IT Drug interactions
(**synergistic**, of enoxaparin and heparin, with alteplase-induced thrombolysis)
IT 9005-49-6, Enoxaparin, biological studies
RL: BIOL (Biological study)
(alteplase thrombolysis potentiation by fractionated and unfractionated)
IT 9002-04-4, Thrombin 9002-05-5, Blood-coagulation **factor Xa**
RL: BIOL (Biological study)
(in alteplase thrombolysis enhancement by enoxaparin and heparin, arterial patency and venous clot lysis in relation to)
IT 105857-23-6, Alteplase
RL: BIOL (Biological study)
(thrombolysis from, enoxaparin and heparin enhancement of, comparison of)

=>

coagulation factor VIIa 65522-14-7, Blood coagulation factor Va 72175-66-7, Blood coagulation factor VIIIa
RL: BSU (Biological study, unclassified); **BIOL (Biological study)** (use of anti-coagulation factor antibodies as long-lasting protective agents)

IT **50-78-2, Acetylsalicylic acid**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (use of anti-coagulation factor antibodies as long-lasting protective agents)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Bajaj; Journal of Biological Chemistry 1985, V260(21), P11574 CAPLUS
(2) Gorog; American Journal of Clinical Pathology 1986, V86(3), P311 CAPLUS
(3) Harker, A; Book of Abstracts, 212th ACS National Meeting, abstract MEDI 109 1996
(4) Sallah, S; Annals of Hematology 1997, V75, P1 CAPLUS
(5) Shapiro; Thrombosis and Haemostasis 1996, V75(1), P30 CAPLUS
(6) Smithkline Beecham Corporation; WO 9726010 A1 1997 CAPLUS

L28 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 1999:458944 CAPLUS
DN 131:78465
TI Antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide
IN Cariou, Roger; Stiekema, Jacobus Christianus Johannes
PA Sanofi, Fr.; Akzo Nobel N.V.
SO Braz. Pedido PI, 19 pp.
CODEN: BPXXDX
DT Patent
LA Portuguese
IC ICM C07H017-04
ICS C07C065-00; A61K031-19; A61K031-715
CC 63-6 (Pharmaceuticals)
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |
| | AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| | AU 9716319 | A1 | 19980917 | | |
| PRAI | BR 1997-1313 | | 19970317 | | |

AB A synthetic oligosaccharide is disclosed which is a selective inhibitor of blood coagulation factor **Xa** and acts via antithrombin III, alone or in combination with **aspirin**, and can be used to prevent or treat thromboembolic diseases related to percutaneous transluminal angioplasty. The oligosaccharide of the invention is O-(2-deoxy-2-sulfoamino-6-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(.beta.-D-glucopyranosyluronic acid)-(1.fwdarw.4)-O-(2-deoxy-2-sulfoamino-3,6-di-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(2-O-sulfo-.alpha.-idopyranosyluronic acid)-(1.fwdarw.4)-1-O-methyl-2-O-sulfoamino-6-O-sulfo-.alpha.-D-glucopyranoside decasodium salt.

ST antiXa oligosaccharide antithrombotic formulation **aspirin**

IT Artery
(angioplasty; antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT Anticoagulants
(antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT Drug delivery systems
(injections, i.v.; antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT Drug delivery systems
(injections, s.c.; antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT 104993-28-4 114870-03-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT **50-78-2, Aspirin**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT 9000-94-6, Antithrombin III
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

IT **9002-05-5**, Factor **xa**
RL: BSU (Biological study, unclassified); **BIOL (Biological study)**
(inhibitors; antithrombotic formulation combining **aspirin** with an anti-**Xa** oligosaccharide)

L28 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 1999:7809 CAPLUS
DN 130:61081
TI Compositions for treating and preventing arterial thrombosis and use of a factor **Xa** inhibitor alone or combined with a platelet aggregation inhibitor

IN Bernat, Andre; Herbert, Jean-Marc; Petitou, Maurice; Van Amsterdam, Ronald
PA Sanofi, Fr.; Akzo Nobel N.V.
SO PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DT Patent
LA French
IC ICM A61K031-00
ICS A61K031-70; A61K031-40; A61K031-70; A61K031-60; A61K031-435; A61K031-445; A61K031-40; A61K031-60; A61K031-435; A61K031-445
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 9856365 | A1 | 19981217 | WO 1998-FR1172 | 19980609 |
| | W: AU, BR, BY, CA, CN, CZ, EE, HU, ID, IL, IS, JP, KR, LK, LT, LV, MX, NO, NZ, PL, RU, SG, SI, SK, TR, UA, US, VN, YU | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | FR 2764511 | A1 | 19981218 | FR 1997-7368 | 19970613 |
| | FR 2764511 | B1 | 20000908 | | |
| | AU 9879246 | A1 | 19981230 | AU 1998-79246 | 19980609 |
| | AU 728826 | B2 | 20010118 | | |
| | EP 986376 | A1 | 20000322 | EP 1998-929521 | 19980609 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | BR 9810520 | A | 20000919 | BR 1998-10520 | 19980609 |
| | JP 2002504110 | T2 | 20020205 | JP 1999-501765 | 19980609 |
| | ZA 9805137 | A | 19990107 | ZA 1998-5137 | 19980612 |
| | NO 9906137 | A | 20000214 | NO 1999-6137 | 19991210 |
| PRAI | FR 1997-7368 | A | 19970613 | | |
| | WO 1998-FR1172 | W | 19980609 | | |

AB Direct or indirect selective inhibitors of factor **Xa** acting via antithrombin III, alone or combined with one or several platelet aggregation inhibitors, are used for prepg. medicines for preventing or treating arterial thromboembolism. Also provided are pharmaceutical compns. contg. one or several direct or indirect selective inhibitors of factor **Xa** acting via antithrombin III in assocn. with one or several platelet aggregation inhibitors, and, optionally one or several pharmaceutically acceptable carriers.

ST antithrombotic factor **Xa** inhibitor platelet aggregation inhibitor; arterial thrombosis factor **Xa** inhibitor platelet aggregation inhibitor; thromboembolism arterial factor **Xa** inhibitor platelet aggregation inhibitor

IT Prosthetic materials and Prosthetics
((endo)vascular; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)

IT Heart, disease
(angina pectoris, unstable; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)

IT Artery
(angioplasty; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)

IT Thrombosis
(arterial; factor **Xa** inhibitor alone or combined with

platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Heart, disease
(auricular fibrillation; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Brain, disease
(cerebrovascular; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Mental disorder
(dementia, ischemic; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Artery
(endarterectomy; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Anticoagulants
Cardiovascular agents
Diabetes mellitus
Drug delivery systems
Drug interactions
Platelet aggregation inhibitors
(factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Dialysis
(hemodialysis; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Brain, disease
Heart, disease
(infarction; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Ischemia
(ischemic dementia; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Artery, disease
(peripheral; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Artery, disease
(restenosis; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Thrombosis
(rethrombosis; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Atherosclerosis
(thromboembolic disorder assocd. with; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Embolism
(thromboembolism; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT Integrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.IIb.beta.3, antagonists; factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)
IT **50-78-2**, **Aspirin** 55142-85-3, Ticlopidine

104993-28-4, SR 90107 113665-84-2, Clopidogrel 114870-03-0
150612-55-8 180144-61-0 190841-78-2 190841-79-3, SR 121787
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)

IT 9000-94-6, Antithrombin III **9002-05-5**, Blood coagulation factor **Xa**
RL: BPR (Biological process); BSU (Biological study, unclassified); **BIOL (Biological study)**; PROC (Process)
(factor **Xa** inhibitor alone or combined with platelet aggregation inhibitor for treatment of arterial thrombosis)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE


(1) Bernat; Fibrinolysis 1996, V10(3), P151 CAPLUS
(2) Cadroy, Y; Thrombosis and Haemostasis V70(4), P631 CAPLUS
(3) Choay; EP 0138632 A 1985 CAPLUS
(4) Daiichi Seiyaku Co; EP 0540051 A 1993 CAPLUS
(5) Fitzgerald; Expert Opin Ther Patents 1995, V5(11), P1143
(6) Fukuda; JPN J Pharmacol 1996, V71(sup 1), P327p
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(8) Herbert; Cardiovasc Drug Rev 1997, V15(1), P1 CAPLUS
(9) Herbert; Circ Res 1996, V79(3), P590 CAPLUS
(10) Herbert; J Pharmacol Exp Ther 1996, V276(3), P1030 CAPLUS
(11) Kaiser; Clin Appl Thromb Hemost 1997, V3(1), P16
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(13) Kunitada; Curr Pharm Design 1996, V2(5), P531 CAPLUS
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(15) Schiele, F; Circulation 1996, V94(8)
(16) van Amsterdam; Thromb Haemost 1997, P2834
(17) Verstraete; Drugs 1995, V49(6), P856 CAPLUS
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(19) Vuillemenot, A; European Heart Journal 1997, V18, P622
(20) Yamashita; Thromb Res 1997, V85(1), P45 CAPLUS
(21) Zandberg; Fibrinolysis 1996, V10(suppl 3), P24

L28 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 1999:401026 CAPLUS
DN 131:35871
TI Compositions containing an association of **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharide optionally in combination with **aspirin**
IN Cariou, Roger; Stiekema, Jacobus
PA Sanofi S. A., Neth.; Akzo Nobel N. V.
SO Pat. Specif. (Aust.), 26 pp.
CODEN: ALXXAP
DT Patent
LA English
IC ICM A61K031-60
ICS A61K031-70
CC 63-6 (Pharmaceuticals)
FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | AU 698456 | B2 | 19981029 | AU 1997-16319 | 19970314 |
| | AU 9716319 | A1 | 19980917 | | |
| | BR 9701313 | A | 19981117 | BR 1997-1313 | 19970317 |
| PRAI | BR 1997-1313 | | 19970317 | | |

AB A method for treatment or prophylaxis of thromboembolic disease assocd. with percutaneous transluminal angioplasty is disclosed which entails administration of an ED of **aspirin** in addn. to an effective quantity of at least one synthetic pentasaccharide which is a selective inhibitor of factor **Xa** and acts via antithrombin III. The pentasaccharide may be O-methyl-(3,4-di-O-methyl-2,6-di-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(3-O-methyl-2-O-sulfo-.beta.-D-glucopyranosyluronic acid)-(1.fwdarw.4)-O-(2,3,6-tri-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(3-O-methyl-2-O-sulfo-.alpha.-L-idopyranosyluronic acid)-(1.fwdarw.4)-2,3,6-tri-O-.alpha.-D-glucopyranoside, O-methyl-(2-deoxy-2-sulfoamino-6-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(.beta.-D-glucopyranosyluronic acid)-(1.fwdarw.4)-O-(2-deoxy-2-sulfoamino-3,6-di-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(2-O-sulfo-.alpha.-L-idopyranosyluronic acid)-(1.fwdarw.4)-2-deoxy-2-sulfoamino-6-O-sulfo-.alpha.-D-glucopyranoside, or O-methyl-(2,3,4-tri-O-methyl-6-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(2,3-di-O-methyl-.beta.-D-glucopyranosyluronic acid)-(1.fwdarw.4)-O-(2,3,6-tri-O-sulfo-.alpha.-D-glucopyranosyl)-(1.fwdarw.4)-O-(2,3-di-O-methyl-.alpha.-L-idopyranosyluronic acid)-(1.fwdarw.4)-2,3,6-tri-O-sulfo-.alpha.-D-glucopyranoside or their decasodium salts.

ST **aspirin** antithrombotic pentasaccharide anti **Xa** angioplasty

IT Artery
(angioplasty, percutaneous transluminal; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Anticoagulants
(antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Drug delivery systems

(injections, i.v.; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Drug delivery systems
(injections, s.c.; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Oligosaccharides, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pentasaccharides; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT Embolism
(thromboembolism; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT **50-78-2**, **Aspirin** 104993-28-4 114870-03-0, SR 90107A 148147-80-2 162610-17-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspirin**)

IT **9002-05-5**, Coagulation factor **Xa**
RL: BSU (Biological study, unclassified); **BIOL (Biological study)**
(inhibitors; antithrombotics contg. **aspirin** and an anti-**Xa** oligosaccharide and use of anti-**Xa** oligosaccharides in combination with **aspiri**

L28 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:900613 CAPLUS
DN 134:56957
TI Preparation of amino acid derivatives as serine protease inhibitors
IN Liebeschuetz, John Walter; Lyons, Amanda Jane; Murray, Christopher William; Rimmer, Andrew David; Young, Stephen Clinton; Camp, Nicholas Paul; Jones, Stuart Donald; Morgan, Phillip John; Richards, Simon James; Wylie, William Alexander; Lively, Sarah Elizabeth; Harrison, Martin James; Waszkowycz, Bohdan; Masters, John Joseph; Wiley, Michael John
PA Eli Lilly and Company, USA; Protherics Molecular Design Limited
SO PCT Int. Appl., 350 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D211-00
CC 34-2 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1
FAN.CNT 12

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000076970 | A2 | 20001221 | WO 2000-GB2296 | 20000613 |
| | WO 2000076970 | A3 | 20010719 | | |
| | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | EP 1192135 | A2 | 20020403 | EP 2000-938912 | 20000613 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI | GB 1999-13823 | A | 19990614 | | |
| | US 1999-142064P | P | 19990702 | | |
| | GB 1999-18741 | A | 19990809 | | |
| | GB 1999-29552 | A | 19991214 | | |
| | GB 1999-29553 | A | 19991214 | | |
| | WO 2000-GB2296 | W | 20000613 | | |

OS MARPAT 134:56957
AB Compds. R2-X-X-Y(Cy)-L-Lp(D)n [R2 represents a 5- or 6-membered arom. carbon ring optionally interrupted by a N, O or S ring atom, optionally substituted at the 3 and/or 4 position or forms a fused ring system at these positions, which is an optionally substituted 5 or 6 membered carbocyclic or heterocyclic ring; X is a C, N, O or S atom or a CO, CR1a, C(R1a)2 or NR1a group, where R1a represents H, OH, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, alkoxyalkyl, alkoxycarbonyl, alkylaminocarbonyl, alkoxycarbonylamino, acyloxymethoxycarbonyl or alkylamino optionally substituted by OH, alkylamino, alkoxy, oxo, aryl or cycloalkyl; L is an org. linker group contg. 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Y is a N atom or a CR1b group (R1b defined as for R1a); Cy is an (un)substituted, (un)satd., mono- or polycyclic, homo- or heterocyclic group; Lp is a lipophilic org. group; D is a hydrogen bond donor group; n = 0-2] were prepd. for use as serine protease inhibitors. Compds. of the invention were found to significantly elongate the partial thromboplastin time (prothrombin time). Thus, 1-(3-amino-2-naphthoyl-D-phenylglycinyl)-4,4'-bispiperidine was prepd. and shown to double the prothrombin time at a concn. of 26 .mu.M.
ST amino acid compd prepn serine protease inhibitor
IT Anticoagulants
(prepn. of amino acid derivs. as serine protease inhibitors)

IT Amino acids, preparation
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT 313489-33-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT 313486-66-7P 313486-67-8P 313486-68-9P 313486-69-0P 313486-70-3P
313486-71-4P 313486-72-5P 313486-73-6P 313486-74-7P 313486-75-8P
313486-76-9P 313486-77-0P 313486-78-1P 313486-79-2P 313486-80-5P
313486-81-6P 313486-82-7P 313486-83-8P 313486-84-9P 313486-85-0P
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313488-86-7P 313488-87-8P 313488-88-9P 313488-89-0P 313488-90-3P
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313488-96-9P 313488-97-0P 313488-98-1P 313488-99-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT 313489-00-8P 313489-01-9P 313489-02-0P 313489-03-1P 313489-04-2P

313489-05-3P 313489-06-4P 313489-07-5P 313489-08-6P 313489-09-7P
313489-10-0P 313489-11-1P 313489-12-2P 313489-13-3P 313489-14-4P
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313492-24-9P 313492-27-2P 313492-30-7P 313492-33-0P 313492-36-3P
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313492-97-6P 313493-00-4P 313493-03-7P 313493-06-0P 313493-08-2P
313493-10-6P 313493-13-9P 313493-16-2P 313493-19-5P 313493-22-0P
313493-25-3P 313493-28-6P 313493-31-1P 313493-33-3P 313690-67-4P
313690-70-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT **9002-05-5**, Factor **xa** 37259-58-8, Serine protease
RL: BPR (Biological process); BSU (Biological study, unclassified); **BIOL (Biological study)**; PROC (Process)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT **50-78-2**, 2-Acetoxybenzoic acid 51-01-4, 2,4-Diacetoxybenzoic acid 56-41-7, L-Alanine, reactions 56-45-1, L-Serine, reactions 60-34-4, Methylhydrazine 62-53-3, Aniline, reactions 67-64-1, Acetone, reactions 72-19-5, L-Threonine, reactions 75-07-0, Acetaldehyde, reactions 75-31-0, Isopropylamine, reactions 79-03-8, Propanoyl chloride 79-30-1, 2-Methylpropanoyl chloride 79-33-4, s 2-Hydroxypropanoic acid, reactions 89-77-0, 4-Chloroanthranilic acid 93-09-4, 2-Naphthalenecarboxylic acid 96-22-0, 3-Pentanone 97-69-8, n-Acetyl-L-Alanine 99-88-7 100-07-2, 4-Methoxybenzoyl chloride 100-09-4, p-Anisic acid 100-43-6, 4-Vinylpyridine 100-52-7, Benzaldehyde, reactions 103-67-3, n-Methylbenzylamine 103-82-2, Phenylacetic acid, reactions 104-84-7, 4-Methylbenzylamine 106-47-8, 4-Chloroaniline, reactions 107-95-9, .beta.-Alanine 107-97-1, Sarcosine 108-12-3, 3-Methylbutanoyl chloride 108-94-1, Cyclohexanone, reactions 108-95-2, Phenol, reactions 109-00-2, 3-Hydroxypyridine 109-89-7, Diethylamine, reactions 109-96-6, 3-Pyrroline 110-89-4, Piperidine, reactions 120-92-3, Cyclopentanone 122-78-1, Phenylacetaldehyde 123-75-1, Pyrrolidine, reactions 124-40-3, Dimethylamine, reactions 127-06-0, Acetoxime 141-97-9, Ethyl acetoacetate 147-85-3, L-Proline, reactions 150-19-6, 3-Methoxyphenol 150-76-5, 4-Methoxyphenol 156-38-7, 4-Hydroxyphenylacetic acid

312-84-5, D-Serine 338-69-2, D-Alanine 344-25-2, D-Proline 367-12-4,
2-Fluorophenol 371-41-5, 4-Fluorophenol 372-20-3, 3-Fluorophenol
399-76-8, 1H-Indole-2-carboxylic acid, 5-fluoro- 462-08-8,
3-Aminopyridine 496-15-1 496-41-3, 2-Benzofurancarboxylic acid
498-94-2, Isonipecotic acid 500-22-1, 3-Pyridinecarboxaldehyde
501-81-5, 3-Pyridylacetic acid 543-24-8, n-Acetylglycine 553-26-4,
4,4'-Bipyridine 580-17-6, 3-Aminoquinoline 586-30-1 589-92-4,
4-Methylcyclohexanone 614-75-5, 2-Hydroxyphenylacetic acid 615-13-4,
2-Indanone 619-80-7, 4-Nitrobenzamide 621-37-4, 3-Hydroxyphenylacetic
acid 626-43-7, 3,5-Dichloroaniline 626-58-4, 4-Methylpiperidine
626-67-5, 1-Methylpiperidine 645-09-0, 3-Nitrobenzamide 645-65-8,
4-Imidazoleacetic acid 766-09-6, 1-Ethylpiperidine 766-79-0,
1-Isopropylpiperidine 872-50-4, n-Methyl-2-pyrrolidinone, reactions
872-85-5, 4-Pyridinecarboxaldehyde 875-74-1, D-Phenylglycine
1072-72-6, Tetrahydro-4h-thiopyran-4-one 1073-29-6, 2-Methylthiophenol
1121-60-4, 2-Pyridinecarboxaldehyde 1436-59-5, cis-1,2-
Diaminocyclohexane 1445-73-4, 1-Methyl-4-piperidinone 1477-50-5,
2-Indolecarboxylic acid 1670-82-2, 6-Indolecarboxylic acid 1734-62-9
2043-61-0, Cyclohexanecarboxaldehyde 2065-66-9,
Methyltriphenylphosphonium iodide 2217-43-8 2359-60-6 2632-13-5,
.alpha.-Bromo-4-methoxyacetophenone 2739-98-2, Ethyl 2-pyridineacetate
2799-21-5 2859-67-8, 3-Pyridinepropanol 2879-79-0 3470-53-9
3470-54-0 3622-04-6, 2-Benzothiazolecarboxylic acid 3731-52-0,
3-Aminomethylpyridine 3731-53-1, 4-Aminomethylpyridine 4066-41-5
4318-37-0 4382-54-1 5116-00-7 5326-23-8 5382-16-1,
4-Hydroxypiperidine 5464-07-3 5794-88-7, 2-Amino-5-bromobenzoic acid
6285-57-0 6314-28-9, Benzo[b]thiophene-2-carboxylic acid 6329-61-9,
Decahydroisoquinoline 6457-49-4, 4-Piperidinemethanol 7409-18-9,
3-Nitrobenzylamine 7697-29-2, 4-Chloro-3-methylbenzoic acid 10241-97-1
10242-08-7 10242-09-8 10242-10-1, 2-Benzofurancarboxylic acid,
5-chloro- 10517-21-2 13293-47-5 13771-75-0 14572-89-5,
1-(4-Aminophenyl)ethanol 14675-99-1 16136-58-6, 1-Methyl-2-
Indolecarboxylic acid 16588-15-1, 2-Chloro-5-nitrobenzamide 16732-73-3
17295-26-0 17336-08-2 17336-11-7 17609-52-8 19436-52-3,
n-Acetyl-D-Alanine 19727-83-4 19810-31-2, 2-Benzyloxyacetyl chloride
20873-58-9 21296-94-6, 2,3-Dimethyl-5-nitroindole 22620-27-5
22818-40-2, D-(4-Hydroxyphenyl)glycine 23995-88-2 24425-40-9
24461-61-8, D-Phenylglycine methyl ester 24673-56-1 26018-73-5
27489-33-4 28286-79-5, 3-Hydroxymethylbenzoic acid 28356-58-3,
4-Pyridylacetic acid 29943-42-8, Tetrahydro-4h-pyran-4-one 30379-55-6
32692-19-6, 2,3-Dihydro-5-nitroindole 33125-05-2 36316-71-9,
2-Chloropyridine hydrochloride 37908-96-6, 3-Chloro-4-methoxybenzoic
acid 40353-34-2 40499-83-0, 3-Hydroxypyrrolidine 50551-61-6
50670-64-9, 3-Cyano-4-methylaniline 51673-84-8, Glyoxal, dimethyl acetal
54401-85-3, Ethyl 4-pyridineacetate 56613-80-0, r-2-Phenylglycinol
56621-48-8 57260-71-6 57479-70-6 60444-56-6 62368-29-0
64465-53-8, 4-Fluoro-3-methoxyaniline 64951-06-0, Imidazo 1,2 a
pyrimidine 2 carboxylic acid ethyl ester 64987-05-9 69026-14-8,
3-Benzyloxybenzoic acid 70679-89-9 75890-68-5 78619-84-8,
4,4'-Bipiperidine dihydrochloride 87120-72-7 88568-95-0 103796-62-9
109384-19-2, 1-tert-Butoxycarbonyl-4-piperidinol 111524-95-9
117445-22-4 133831-28-4 144222-22-0 156407-78-2 171050-06-9
201286-69-3 219508-17-5 313489-97-3 313490-06-1 313490-07-2
313490-08-3 313490-26-5 313490-39-0 313490-40-3 313490-41-4
313490-80-1 313490-98-1 313493-38-8 313493-40-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of amino acid derivs. as serine protease inhibitors)

IT 89-98-5P, 2-Chlorobenzaldehyde 1200-05-1P 1802-16-0P,
3-Pyridinepropanal 5407-51-2P, 2,6-Benzothiazolediamine 5408-04-8P
5462-71-5P 5623-81-4P, Cyclopentaneacetaldehyde 7188-38-7P, tert-Butyl
isonitrile 15336-72-8P, 4,4'-Bipiperidine 17477-46-2P 40512-48-9P
40512-57-0P 41841-16-1P 42965-35-5P 50382-11-1P 50382-30-4P
52798-01-3P 54817-91-3P 57591-61-4P 64951-10-6P, Imidazo 1,2 a

pyrimidine 2 carboxylic acid 71420-92-3P 71721-67-0P 71721-69-2P
74864-32-7P 76687-25-7P 76687-26-8P 76687-27-9P 79287-71-1P
79608-48-3P 84358-13-4P 99767-45-0P 101385-93-7P 102089-74-7P
102089-75-8P 109431-87-0P 112162-11-5P 117722-19-7P 120690-80-4P,
4-Pyridinepropanal 123855-51-6P 134557-76-9P 137076-22-3P
138891-54-0P 141518-55-0P 142121-93-5P 142121-94-6P 161330-30-9P
191871-32-6P 214698-07-4P 214698-09-6P 221050-85-7P 313489-93-9P
313489-94-0P 313489-95-1P 313489-96-2P 313489-98-4P 313489-99-5P
313490-00-5P 313490-01-6P 313490-02-7P 313490-03-8P 313490-04-9P
313490-05-0P 313490-09-4P 313490-10-7P 313490-11-8P 313490-12-9P
313490-13-0P 313490-14-1P 313490-15-2P 313490-16-3P 313490-17-4P
313490-18-5P 313490-19-6P 313490-20-9P 313490-21-0P 313490-22-1P
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313490-47-0P 313490-48-1P 313490-49-2P 313490-50-5P 313490-51-6P
313490-52-7P 313490-53-8P 313490-54-9P 313490-55-0P 313490-56-1P
313490-57-2P 313490-58-3P 313490-59-4P 313490-60-7P 313490-61-8P
313490-62-9P 313490-63-0P 313490-64-1P 313490-65-2P 313490-67-4P
313490-68-5P 313490-69-6P 313490-70-9P 313490-72-1P 313490-73-2P
313490-74-3P 313490-75-4P 313490-76-5P 313490-77-6P 313490-78-7P
313490-79-8P 313490-81-2P 313490-82-3P 313490-83-4P 313490-84-5P
313490-85-6P 313490-86-7P 313490-87-8P 313490-88-9P 313490-89-0P
313490-90-3P 313490-91-4P 313490-92-5P 313490-93-6P 313490-94-7P
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313491-01-9P 313491-02-0P 313491-04-2P 313491-05-3P 313491-06-4P
313491-07-5P 313491-09-7P 313491-10-0P 313491-11-1P 313491-12-2P
313491-13-3P 313491-14-4P 313491-15-5P 313491-16-6P 313491-17-7P
313491-18-8P 313491-19-9P 313491-20-2P 313491-21-3P 313491-22-4P
313491-23-5P 313491-24-6P 313491-25-7P 313491-26-8P 313491-27-9P
313491-28-0P 313491-29-1P 313491-30-4P 313491-31-5P 313491-32-6P
313491-33-7P 313491-34-8P 313493-37-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of amino acid derivs. as serine protease inhibitors)

L28 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:728390 CAPLUS
DN 134:13215
TI Nonpeptide factor **Xa** inhibitors. II. Antithrombotic evaluation in a rabbit model of electrically induced carotid artery thrombosis
AU Wong, Pancras C.; Crain, Earl J.; Knabb, Robert M.; Meade, Raymond P.; Quan, Mimi L.; Watson, Carol A.; Wexler, Ruth R.; Wright, Matthew R.; Slee, Andrew M.
CS Cardiovascular Diseases Research, DuPont Pharmaceuticals Company, Wilmington, DE, USA
SO Journal of Pharmacology and Experimental Therapeutics (2000), 295(1), 212-218
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-8 (Pharmacology)
AB SK549 (mol. wt. 546 Da) is a synthetic, selective inhibitor of human coagulation factor **Xa** (fXa) (Ki = 0.52 nM). This study compared the antithrombotic effects of SK549 and a series of benzamidine isoxazoline fXa inhibitors with **aspirin**, DuP 714 (a direct thrombin inhibitor), recombinant tick anticoagulant peptide, or heparin in a rabbit model of elec. induced carotid arterial thrombosis. Compds. were infused i.v. continuously from 60 min before elec. stimulation to the end of the expt. Values of ED50 (dose that increases the carotid blood flow to 50% of the control) were 0.12 .mu.mol/kg/h for SK549, 0.56 .mu.mol/kg/h

for **aspirin**, 0.14 .mu.mol/kg/h for DuP 714, 0.06 .mu.mol/kg/h for recombinant tick anticoagulant peptide, and >100 U/kg/h for heparin. The EC50 (plasma concn. that increased blood flow to 50% of the control) for SK549 was 97 nM. Unlike **aspirin** and heparin, SK549 was efficacious and, at 1.5 .mu.mol/kg/h i.v. (n = 9), maintained carotid blood flow at 87.+-.6% of control level for greater than 90 min. Unlike heparin, SK549 inhibited ex vivo fXa activity but not ex vivo thrombin activity. There was a highly significant correlation between Ki (fXa) and ED50 of a series of fXa inhibitors (r = 0.85, P <.001). Therefore, these results suggest that SK549 is a novel, potent, and effective antithrombotic agent in a rabbit model of arterial thrombosis. It is likely that SK549 exerts its antithrombotic effect through selective inhibition of fXa. Furthermore, SK549 may be clin. useful for the prevention of arterial thrombosis.

ST blood coagulation inhibitor antithrombotic artery thrombosis; SK549 antithrombotic coronary circulation artery thrombosis

IT Anticoagulants
(antithrombotic evaluation of SK549 and nonpeptide factor **Xa** inhibitors in a rabbit model of elec. induced carotid artery thrombosis)

IT Circulation
(coronary; antithrombotic evaluation of SK549 and nonpeptide factor **Xa** inhibitors in a rabbit model of elec. induced carotid artery thrombosis)

IT 193003-99-5 193004-60-3 193004-63-6 193004-64-7 193004-82-9 193004-83-0 193004-94-3 193004-96-5 231300-13-3, SK 549
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antithrombotic evaluation of SK549 and nonpeptide factor **Xa** inhibitors in a rabbit model of elec. induced carotid artery thrombosis)

IT 9002-04-4, Thrombin **9002-05-5**, Blood-coagulation factor **Xa**
RL: BPR (Biological process); BSU (Biological study, unclassified); **BIOL (Biological study)**; PROC (Process)
(antithrombotic evaluation of SK549 and nonpeptide factor **Xa** inhibitors in a rabbit model of elec. induced carotid artery thrombosis)

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD

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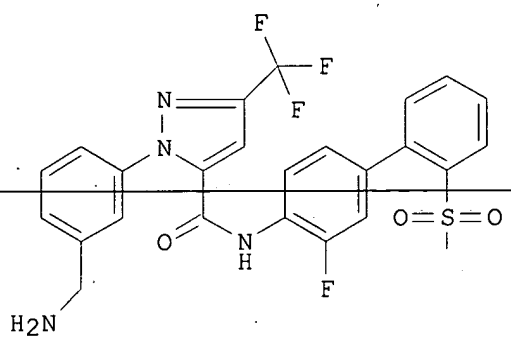
L28 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:645898 CAPLUS
DN 133:232835
TI Treatment of thrombosis by combined use of a factor **xa** inhibitor and **aspirin**, tissue plasminogen activator (TPA), a GPIIb/IIIa antagonist, low molecular weight heparin or heparin
IN Wong, Pancras C.
PA Du Pont Pharmaceuticals Company, USA
SO PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61P007-02
ICS A61P009-12; A61K031-715; A61K045-06; A61K038-49; A61K038-02; A61K031-42; A61K031-60; A61K038-49; A61K031-415; A61K038-02; A61K031-415; A61K045-06; A61K031-715; A61K031-415; A61K031-60; A61K031-415; A61K031-42; A61K031-415
CC 1-8 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000053264 | A1 | 20000914 | WO 2000-US6451 | 20000310 |
| | W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| | EP 1161279 | A1 | 20011212 | EP 2000-913894 | 20000310 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| | BR 2000010381 | A | 20020205 | BR 2000-10381 | 20000310 |
| PRAI | US 1999-123815P | P | 19990311 | | |
| | WO 2000-US6451 | W | 20000310 | | |

GI



I

AB Provided is a method of treating thrombosis in mammals by administering therapeutically effective amts. of a combination of (i) a Factor **Xa** inhibitor, and (ii) a compd. selected from the group consisting of **aspirin**, TPA, a GPIIb/IIIa antagonist, low mol. wt. heparin and heparin, wherein the dose administered for at least one of (i) and (ii) is a subtherapeutic dose. Preferably, the combination of (i) and (ii) provides a synergistic effect. A combination of I (Factor **Xa** inhibitor) and **aspirin** at their subtherapeutic doses produced a significant antithrombotic effect in a rabbit model of arterial thrombosis. Pharmaceutical dosage forms are discussed.

ST antithrombotic factor **Xa** inhibitor

IT Anticoagulants
Drug delivery systems
(antithrombotic combination of a Factor **Xa** inhibitor and **aspirin**, TPA, a GPIIb/IIIa antagonist, or heparin deriv.)

IT Drug interactions
(synergistic; antithrombotic combination of a Factor **Xa** inhibitor and **aspirin**, TPA, a GPIIb/IIIa antagonist, or heparin deriv.)

IT Integrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.IIb.beta.3, antagonists; antithrombotic combination of a Factor **Xa** inhibitor and **aspirin**, TPA, a GPIIb/IIIa antagonist, or heparin deriv.)

IT **50-78-2** 9005-49-6, Heparin, biological studies 139639-23-9, Tissue plasminogen activator 185536-58-7D, salt 209955-61-3 209957-48-2 292135-59-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antithrombotic combination of a Factor **Xa** inhibitor and **aspirin**, TPA, a GPIIb/IIIa antagonist, or heparin deriv.)

IT **9002-05-5**, Factor **Xa**
RL: BSU (Biological study, unclassified); **BIOL (Biological study)**
(inhibitors; antithrombotic combination of a Factor **Xa** inhibitor and **aspirin**, TPA, a GPIIb/IIIa antagonist, or heparin deriv.)

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD

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(4) Du Pont Merck Pharma; WO 9828269 A 1998 CAPLUS
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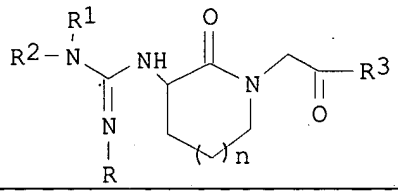
(9) Merck & Co Inc; WO 9945913 A 1999 CAPLUS

(10) Squibb Bristol Myers Co; EP 0832879 A 1998 CAPLUS

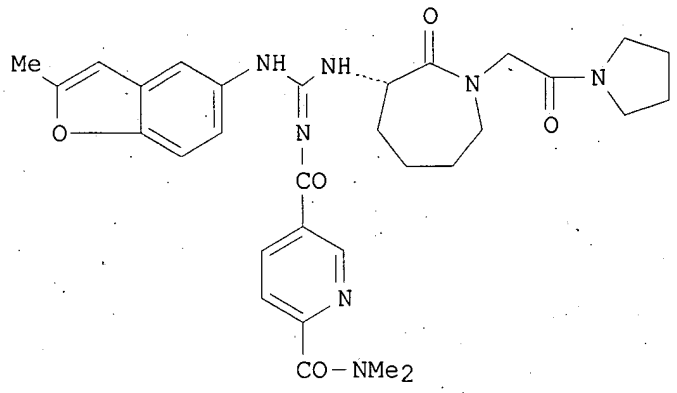
L28 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:573666 CAPLUS
DN 133:164010
TI Preparation of caprolactams, piperidinones, and pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals
IN Stein, Philip D.; Bisacchi, Gregory S.; Shi, Yan; O'Connor, Stephen P.; Li, Chi
PA Bristol-Myers Squibb Company, USA
SO PCT Int. Appl., 284 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-40
ICS A61K031-4015; A61K031-4412; A61P007-00; A61P009-00; C07D401-06; C07D403-06
CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 63
FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|---|
| PI | WO 2000047207 | A1 | 20000817 | WO 2000-US2883 | 20000202 |
| | W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | US 6297233 | B1 | 20011002 | US 2000-496571 | 20000202 |
| | EP 1156803 | A1 | 20011128 | EP 2000-914505 | 20000202 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI | US 1999-119372P | P | 19990209 | | |
| | US 1999-167428P | P | 19991124 | | |
| | WO 2000-US2883 | W | 20000202 | | |

OS MARPAT 133:164010
GI



I



II

AB Title chiral compds. [I; R = CN, CONH2, COOCH2CH3, COC6H5, SO2NH2, OCH3, SO2N(CH3)2, SO2CH3, arylsulfonyl, heterocyclosulfonyl, (un)substituted Ph, heterocyclyl, heterocycleocarbonyl, alkoxylcarbonyl, arylaminocarbonyl; R1 = H, arylalkyl; R2 = alkyl, (un)substituted Ph, benzoheterocyclyl, cyclopentyl; R3 = heterocyclylamino, heterocyclyl, alkoxy, cycloalkylamino, OH; n = 0, 1, 2] , pharmaceutically acceptable salts, and stereoisomers are pred. as Factor **Xa** inhibitors and are useful as anticoagulants (no data). A method for treating cardiovascular diseases assocd. with thromboses is also provided. Thus, the title compd. II was prepd.

ST caprolactam Factor **Xa** inhibitor prepn anticoagulant cardiovascular agent; piperidinone prepn Factor **Xa** inhibitor; pyrrolidinone prepn Factor **Xa** inhibitor

IT Anticoagulants
Cardiovascular agents
Mammal (Mammalia)
(prepn. of caprolactams, piperidinones, and pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT Sulfonamides
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of caprolactams, piperidinones, and pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT Antihypertensives
Thromboxane receptor antagonists
(prepn. of pharmaceutical combination with caprolactams in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT Prostacyclin receptors
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(prepn. of pharmaceutical combination with caprolactams in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288075-36-5P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzocaprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 108-44-1, 3-Methylaniline, reactions 288083-19-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of caprolactams and piperidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 75-64-9, tert-Butylamine, reactions 93-97-0, Benzoic anhydride 96-32-2, Methyl bromoacetate 96-50-4, 2-Aminothiazole 98-97-5, Pyrazinecarboxylic acid 107-10-8, Propylamine, reactions 109-01-3, 1-Methylpiperazine 110-70-3, N,N'-Dimethyl-ethylenediamine 122-04-3, 4-Nitrobenzoyl chloride 123-75-1, Pyrrolidine, reactions 127-06-0, Acetone oxime 138-41-0, 4-(Aminosulfonyl)benzoic acid 350-46-9, 1-Fluoro-4-nitrobenzene 369-34-6, 3,4-Difluoronitrobenzene 461-82-5, 4-(Trifluoromethoxy)aniline 462-08-8, 3-Pyridinamine 501-53-1, Benzyl chloroformate 504-29-0, 2-Aminopyridine 586-38-9, 3-Methoxybenzoic acid 614-69-7, (2-Methyl)phenyl isothiocyanate 621-30-7, (3-Methylphenyl)isothiocyanate 622-08-2, 2-Benzyloxyethanol 624-83-9, Methyl isocyanate 667-24-3 694-05-3, 1,2,3,6-Tetrahydropyridine 881-86-7, Dimethyl 2,5-pyridinedicarboxylate 937-14-4, 3-Chloroperbenzoic acid 1636-33-5, 2-Naphthylisothiocyanate 2243-83-6, 2-Naphthoyl chloride 2439-77-2, 2-Methoxybenzamide 2466-76-4, N-Acetylimidazole 2759-28-6, 1-Benzylpiperazine 3010-82-0, 1,4-Benzenedicarboxamide 3662-78-0, Methyl 4-isothiocyanatobenzoate 4039-32-1, Lithium bis(trimethylsilyl)amide 5437-45-6, Benzyl bromoacetate 5638-76-6 13078-79-0, 3-Chlorobenzeneethanamine 13382-43-9, 2-Methyl-5-benzothiazolamine 16182-04-0, Ethoxycarbonyl isothiocyanate 19981-17-0, Sodium cyanamide 21568-87-6 22118-09-8, Bromoacetyl chloride 23968-37-8, 2-Methyl-5-benzofuranamine hydrochloride 25660-70-2 26210-75-3, 2-Methyl-5-benzofuranamine 28675-14-1, N,N'-Dimethylbenzenediamine 32955-21-8, Ethyl 2-amino-5-thiazolecarboxylate 36397-23-6, 4-Methoxy-benzenepropanamine 37718-11-9, 4-Pyrazolecarboxylic acid 40033-49-6 66090-36-6, 3-Chlorobenzoyl isothiocyanate 69941-33-9, Benzenedicarboxamide 70654-85-2 72745-76-7, 2-Methyl-5-benzoxazolamine 76944-95-1 79463-77-7, Diphenyl cyanocarbonimidate 79839-29-5 82846-28-4 83527-99-5, 2-Amino-6H-dibenzo[b,d]pyran-6-one 84358-13-4, 1,4-Piperidinedicarbosylic acid 1-(1,1-dimethylethyl) ester 87977-31-9, 2-Methyl-6-nitrobenzofuran 90892-09-4, 1-(Bromoacetyl)pyrrolidine 106691-72-9 126417-82-1, 1-Methyl-3-(4-chlorophenyl)pyrazol-5-amine 152839-22-0 159465-27-7 162468-78-2 190141-99-2, tert-Butyl 3-amino-4-hydroxy-1-pyrrolidinecarboxylate 288082-90-6 288083-15-8 288083-16-9 288083-24-9 288083-36-3 288083-80-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 13680-03-0P, 2-Propanone O-(4-nitrophenyl)oxime 14146-09-9P, 2-Methyl-5-nitrobenzofuran 28439-70-5P 60557-54-2P 93961-04-7P 103478-12-2P 130228-96-5P 173371-37-4P 288074-84-0P 288082-91-7P 288083-17-0P 288083-18-1P 288083-20-5P 288083-21-6P 288083-22-7P 288083-23-8P, 2-Methyl-6-aminobenzofuran 288083-25-0P 288083-26-1P 288083-27-2P 288083-28-3P, 4-Fluoro-2-methyl-5-nitrobenzofuran 288083-29-4P, 6-Fluoro-2-methyl-5-nitrobenzofuran 288083-30-7P, 4-Fluoro-2-methyl-7-nitrobenzofuran 288083-31-8P, 4-Fluoro-2-methyl-5-aminobenzofuran 288083-32-9P 288083-33-0P 288083-34-1P 288083-35-2P 288083-37-4P 288083-38-5P 288083-39-6P 288083-40-9P 288083-41-0P 288083-42-1P 288083-43-2P 288083-44-3P 288083-45-4P 288083-47-6P, 2-Methyl-3-nitro-5-benzofuranamine 288083-48-7P 288083-49-8P 288083-50-1P 288083-51-2P 288083-52-3P 288083-53-4P 288083-54-5P 288083-56-7P 288083-57-8P 288083-58-9P 288083-59-0P 288083-60-3P 288083-61-4P 288083-62-5P 288083-63-6P 288083-65-8P

288083-66-9P 288083-67-0P 288083-69-2P 288083-71-6P 288083-72-7P
288083-73-8P 288083-75-0P 288083-76-1P 288083-77-2P 288083-78-3P
288083-79-4P 288083-81-8P 288083-82-9P 288083-83-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288074-98-6P 288075-54-7P 288077-92-9P 288078-14-8P 288078-41-1P
288078-58-0P 288078-66-0P 288079-24-3P 288079-60-7P 288079-76-5P
288079-91-4P 288080-49-9P 288082-58-6P 288082-62-2P 288083-95-4P
288084-12-8P 288084-20-8P
RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288074-71-5P 288074-72-6P 288074-73-7P 288074-74-8P 288074-75-9P
288074-76-0P 288074-77-1P 288074-78-2P 288074-79-3P 288074-80-6P
288074-81-7P 288074-82-8P 288074-85-1P 288074-86-2P 288074-87-3P
288074-88-4P 288074-97-5P 288074-99-7P 288075-00-3P 288075-01-4P
288075-02-5P 288075-03-6P 288075-04-7P 288075-05-8P 288075-06-9P
288075-07-0P 288075-08-1P 288075-09-2P 288075-10-5P 288075-11-6P
288075-12-7P 288075-13-8P 288075-14-9P 288075-15-0P 288075-16-1P
288075-17-2P 288075-18-3P 288075-19-4P 288075-20-7P 288075-21-8P
288075-22-9P 288075-23-0P 288075-24-1P 288075-25-2P 288075-26-3P
288075-27-4P 288075-28-5P 288075-29-6P 288075-30-9P 288075-31-0P
288075-37-6P 288075-38-7P 288075-39-8P 288075-40-1P 288075-41-2P
288075-42-3P 288075-43-4P 288075-44-5P 288075-45-6P 288075-46-7P
288075-47-8P 288075-48-9P 288075-49-0P 288075-50-3P 288075-51-4P
288075-52-5P 288075-53-6P 288075-55-8P 288075-56-9P 288075-57-0P
288075-58-1P 288075-59-2P 288075-60-5P 288075-61-6P 288075-62-7P
288075-63-8P 288075-64-9P 288075-65-0P 288075-66-1P 288075-67-2P
288075-68-3P 288075-69-4P 288075-70-7P 288075-71-8P 288075-72-9P
288075-73-0P 288075-74-1P 288075-75-2P 288075-76-3P 288075-77-4P
288075-78-5P 288075-79-6P 288075-80-9P 288075-81-0P 288075-82-1P
288075-83-2P 288075-84-3P 288075-85-4P 288075-86-5P 288075-87-6P
288075-88-7P 288075-89-8P 288075-90-1P 288075-91-2P 288075-92-3P
288075-93-4P 288075-94-5P 288075-95-6P 288075-96-7P 288075-97-8P
288075-98-9P 288075-99-0P 288076-00-6P 288076-01-7P 288076-02-8P
288076-03-9P 288076-04-0P 288076-05-1P 288076-06-2P 288076-07-3P
288076-08-4P 288076-09-5P 288076-10-8P 288076-11-9P 288076-12-0P
288076-13-1P 288076-14-2P 288076-15-3P 288076-16-4P 288076-17-5P
288076-18-6P 288076-19-7P 288076-20-0P 288076-21-1P 288076-22-2P
288076-23-3P 288076-24-4P 288076-25-5P 288076-26-6P 288076-27-7P
288076-28-8P 288076-29-9P 288076-30-2P 288076-31-3P 288076-32-4P
288076-33-5P 288076-34-6P 288076-35-7P 288076-36-8P 288076-37-9P
288076-38-0P 288076-39-1P 288076-40-4P 288076-41-5P 288076-42-6P
288076-43-7P 288076-44-8P 288076-45-9P 288076-46-0P 288076-47-1P
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288076-53-9P 288076-54-0P 288076-55-1P 288076-56-2P 288076-57-3P
288076-58-4P 288076-59-5P 288076-60-8P 288076-61-9P 288076-62-0P
288076-63-1P 288076-64-2P 288076-65-3P 288076-66-4P 288076-67-5P
288076-68-6P 288076-69-7P 288076-70-0P 288076-71-1P 288076-72-2P
288076-73-3P 288076-74-4P 288076-75-5P 288076-76-6P 288076-77-7P
288076-78-8P 288076-79-9P 288076-80-2P 288076-81-3P 288076-82-4P
288076-83-5P 288076-84-6P 288076-85-7P 288076-86-8P 288076-87-9P
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288077-03-2P 288077-04-3P 288077-05-4P 288077-06-5P 288077-07-6P
288077-08-7P 288077-09-8P 288077-10-1P 288077-11-2P 288077-12-3P

288077-13-4P 288077-14-5P 288077-15-6P 288077-16-7P 288077-17-8P
288077-18-9P 288077-19-0P 288077-20-3P 288077-21-4P 288077-22-5P
288077-23-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288077-24-7P 288077-25-8P 288077-26-9P 288077-27-0P 288077-28-1P
288077-29-2P 288077-30-5P 288077-31-6P 288077-32-7P 288077-33-8P
288077-34-9P 288077-35-0P 288077-36-1P 288077-37-2P 288077-38-3P
288077-39-4P 288077-40-7P 288077-41-8P 288077-42-9P 288077-43-0P
288077-44-1P 288077-45-2P 288077-46-3P 288077-47-4P 288077-48-5P
288077-49-6P 288077-50-9P 288077-51-0P 288077-52-1P 288077-53-2P
288077-54-3P 288077-55-4P 288077-56-5P 288077-57-6P 288077-58-7P
288077-59-8P 288077-60-1P 288077-61-2P 288077-62-3P 288077-63-4P
288077-64-5P 288077-65-6P 288077-66-7P 288077-67-8P 288077-68-9P
288077-69-0P 288077-70-3P 288077-71-4P 288077-72-5P 288077-73-6P
288077-74-7P 288077-75-8P 288077-76-9P 288077-77-0P 288077-78-1P
288077-79-2P 288077-80-5P 288077-81-6P 288077-82-7P 288077-83-8P
288077-84-9P 288077-85-0P 288077-86-1P 288077-87-2P 288077-88-3P
288077-89-4P 288077-90-7P 288077-91-8P 288077-93-0P 288077-94-1P
288077-95-2P 288077-96-3P 288077-97-4P 288077-98-5P 288077-99-6P
288078-00-2P 288078-01-3P 288078-02-4P 288078-03-5P 288078-04-6P
288078-05-7P 288078-06-8P 288078-07-9P 288078-08-0P 288078-09-1P
288078-10-4P 288078-11-5P 288078-12-6P 288078-13-7P 288078-15-9P
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288078-31-9P 288078-32-0P 288078-33-1P 288078-34-2P 288078-35-3P
288078-36-4P 288078-37-5P 288078-38-6P 288078-39-7P 288078-40-0P
288078-42-2P 288078-43-3P 288078-44-4P 288078-45-5P 288078-46-6P
288078-47-7P 288078-48-8P 288078-49-9P 288078-50-2P 288078-51-3P
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288078-57-9P 288078-59-1P 288078-60-4P 288078-61-5P 288078-62-6P
288078-63-7P 288078-64-8P 288078-65-9P 288078-67-1P 288078-68-2P
288078-69-3P 288078-70-6P 288078-71-7P 288078-72-8P 288078-73-9P
288078-74-0P 288078-75-1P 288078-76-2P 288078-77-3P 288078-78-4P
288078-79-5P 288078-81-9P 288078-83-1P 288078-85-3P 288078-87-5P
288078-89-7P 288078-91-1P 288078-93-3P 288078-95-5P 288078-97-7P
288078-99-9P 288079-01-6P 288079-03-8P 288079-05-0P 288079-07-2P
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288079-37-8P 288079-38-9P 288079-39-0P 288079-40-3P 288079-41-4P
288079-42-5P 288079-43-6P 288079-44-7P 288079-45-8P 288079-46-9P
288079-47-0P 288079-48-1P 288079-49-2P 288079-50-5P 288079-51-6P
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288079-80-1P 288079-81-2P 288079-82-3P 288079-83-4P 288079-84-5P
288079-85-6P 288079-86-7P 288079-87-8P 288079-88-9P 288079-89-0P
288079-90-3P 288079-92-5P 288079-93-6P 288079-94-7P 288079-95-8P
288079-96-9P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288079-97-0P 288079-98-1P 288079-99-2P 288080-00-2P 288080-01-3P
288080-02-4P 288080-03-5P 288080-04-6P 288080-05-7P 288080-06-8P

288080-07-9P 288080-08-0P 288080-09-1P 288080-10-4P 288080-11-5P
288080-12-6P 288080-13-7P 288080-14-8P 288080-15-9P 288080-16-0P
288080-17-1P 288080-18-2P 288080-20-6P 288080-21-7P 288080-22-8P
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288080-28-4P 288080-30-8P 288080-31-9P 288080-32-0P 288080-33-1P
288080-34-2P 288080-35-3P 288080-36-4P 288080-37-5P 288080-38-6P
288080-39-7P 288080-40-0P 288080-41-1P 288080-42-2P 288080-43-3P
288080-44-4P 288080-45-5P 288080-46-6P 288080-47-7P 288080-50-2P
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288080-61-5P 288080-62-6P 288080-63-7P 288080-64-8P 288080-65-9P
288080-66-0P 288080-67-1P 288080-68-2P 288080-69-3P 288080-70-6P
288080-71-7P 288080-72-8P 288080-73-9P 288080-74-0P 288080-75-1P
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288080-81-9P 288080-82-0P 288080-83-1P 288080-84-2P 288080-85-3P
288080-86-4P 288080-87-5P 288080-88-6P 288080-89-7P 288080-90-0P
288080-91-1P 288080-92-2P 288080-93-3P 288080-94-4P 288080-95-5P
288080-96-6P 288080-97-7P 288080-98-8P 288080-99-9P 288081-00-5P
288081-01-6P 288081-02-7P 288081-03-8P 288081-04-9P 288081-05-0P
288081-06-1P 288081-07-2P 288081-08-3P 288081-09-4P 288081-10-7P
288081-11-8P 288081-12-9P 288081-13-0P 288081-14-1P 288081-15-2P
288081-16-3P 288081-17-4P 288081-18-5P 288081-19-6P 288081-20-9P
288081-21-0P 288081-22-1P 288081-23-2P 288081-24-3P 288081-25-4P
288081-26-5P 288081-27-6P 288081-28-7P 288081-29-8P 288081-30-1P
288081-31-2P 288081-32-3P 288081-33-4P 288081-34-5P 288081-35-6P
288081-36-7P 288081-37-8P 288081-38-9P 288081-39-0P 288081-40-3P
288081-41-4P 288081-42-5P 288081-43-6P 288081-44-7P 288081-45-8P
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288081-56-1P 288081-57-2P 288081-58-3P 288081-59-4P 288081-60-7P
288081-61-8P 288081-62-9P 288081-63-0P 288081-64-1P 288081-65-2P
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288081-76-5P 288081-77-6P 288081-78-7P 288081-79-8P 288081-80-1P
288081-81-2P 288081-82-3P 288081-83-4P 288081-84-5P 288081-85-6P
288081-86-7P 288081-87-8P 288081-88-9P 288081-89-0P 288081-90-3P
288081-91-4P 288081-92-5P 288081-93-6P 288081-94-7P 288081-95-8P
288081-96-9P 288081-97-0P 288081-98-1P 288081-99-2P 288082-00-8P
288082-01-9P 288082-02-0P 288082-03-1P 288082-04-2P 288082-05-3P
288082-06-4P 288082-07-5P 288082-08-6P 288082-09-7P 288082-10-0P
288082-11-1P 288082-12-2P 288082-13-3P 288082-14-4P 288082-15-5P
288082-16-6P 288082-17-7P 288082-18-8P 288082-19-9P 288082-20-2P
288082-21-3P 288082-22-4P 288082-23-5P 288082-24-6P 288082-25-7P
288082-26-8P 288082-27-9P 288082-28-0P 288082-29-1P 288082-30-4P
288082-31-5P 288082-32-6P 288082-33-7P 288082-34-8P 288082-35-9P
288082-36-0P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288082-37-1P 288082-38-2P 288082-39-3P 288082-40-6P 288082-41-7P
288082-42-8P 288082-43-9P 288082-44-0P 288082-45-1P 288082-46-2P
288082-47-3P 288082-48-4P 288082-49-5P 288082-50-8P 288082-51-9P
288082-52-0P 288082-53-1P 288082-54-2P 288082-55-3P 288082-56-4P
288082-57-5P 288082-59-7P 288082-60-0P 288082-61-1P 288082-63-3P
288082-64-4P 288082-65-5P 288082-66-6P 288082-67-7P 288082-68-8P
288082-69-9P 288082-70-2P 288082-71-3P 288082-72-4P 288082-73-5P
288082-74-6P 288082-75-7P 288082-76-8P 288082-77-9P 288082-78-0P
288082-79-1P 288082-80-4P 288082-81-5P 288082-82-6P 288082-83-7P
288082-84-8P 288082-85-9P 288082-86-0P 288082-87-1P 288082-88-2P
288082-89-3P 288082-92-8P 288082-93-9P 288082-94-0P 288082-95-1P
288082-96-2P 288082-97-3P 288082-98-4P 288082-99-5P 288083-00-1P

288083-01-2P 288083-02-3P 288083-03-4P 288083-04-5P 288083-05-6P
288083-06-7P 288083-07-8P 288083-08-9P 288083-09-0P 288083-10-3P
288083-11-4P 288083-12-5P 288083-13-6P 288083-14-7P 288083-84-1P
288083-85-2P 288083-86-3P 288083-87-4P 288083-88-5P 288083-89-6P
288083-90-9P 288083-91-0P 288083-92-1P 288083-93-2P 288083-94-3P
288083-96-5P 288083-97-6P 288083-98-7P 288083-99-8P 288084-00-4P
288084-01-5P 288084-02-6P 288084-03-7P 288084-04-8P 288084-05-9P
288084-06-0P 288084-07-1P 288084-08-2P 288084-09-3P 288084-10-6P
288084-11-7P 288084-13-9P 288084-14-0P 288084-15-1P 288084-16-2P
288084-17-3P 288084-18-4P 288084-19-5P 288084-21-9P 288084-22-0P
288084-23-1P 288084-24-2P 288084-25-3P 288084-26-4P 288084-27-5P
288084-28-6P 288084-29-7P 288084-30-0P 288084-31-1P 288084-32-2P
288084-33-3P 288084-34-4P 288084-35-5P 288084-36-6P 288093-54-9P
288093-55-0P 288093-56-1P 288149-15-5P 288149-16-6P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of caprolactams as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT **9002-05-5**, Factor **Xa**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); **BIOL (Biological study)**; OCCU (Occurrence)
(prepn. of caprolactams, piperidinones, and pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT **50-78-2** 58-32-2, Dipyridamole 81-81-2, Warfarin 9002-01-1, Streptokinase 9003-53-6, ASPAC 9039-53-6, Urokinase 32828-81-2, Picotamide 55142-85-3, Ticlopidine 73963-72-1, Cilostazol 74050-98-9, Ketanserin 82657-92-9, Prourokinase 105857-23-6, Activase 105913-11-9D, Plasminogen activator, animal salivary gland 113665-84-2, Clopidogrel 143443-90-7, Ifetroban 152815-51-5 156867-02-6 171870-23-8, Lanoteplase
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(prepn. of pharmaceutical combination with caprolactams in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 92235-39-7, 1,1-Dimethylethyl ((S)-oxo-3-piperidinyl)carbamate
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of piperidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288074-89-5P 288074-90-8P 288074-91-9P 288074-92-0P 288075-32-1P 288075-33-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of piperidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 92235-34-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

IT 288074-93-1P 288074-94-2P 288074-95-3P 288074-96-4P 288075-34-3P 288075-35-4P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrolidinones as Factor **Xa** inhibitors in prevention or treatment of thromboses, coronary artery disease, or cerebrovascular disease in mammals)

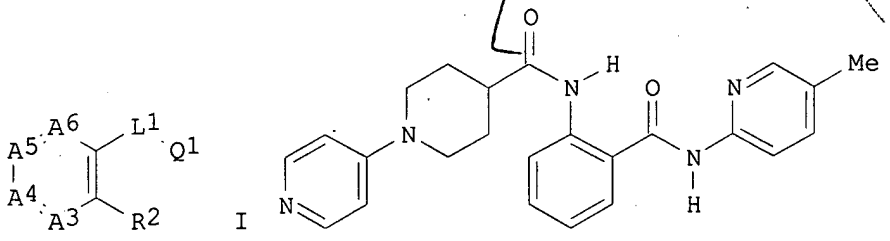
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

(1) Lowe; US 5484917 A 1996 CAPLUS
(2) Lowe; US 5618811 A 1997 CAPLUS

L28 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2002 ACS
AN 2000:457059 CAPLUS
DN 133:89437
TI Preparation of heteroaryl-substituted aromatic amides as factor **Xa** inhibitors
IN Beight, Douglas Wade; Craft, Trelia Joyce; Denny, Carl Penman; Franciskovich, Jeffry Bernard; Goodson, Theodore, Jr.; Hall, Steven Edward; Herron, David Kent; Joseph, Sajan Pariyadan; Klimkowski, Valentine Joseph; Masters, John Joseph; Mendel, David; Milot, Guy; Pineiro-Nunez, Marta Maria; Sawyer, Jason Scott; Shuman, Robert Theodore; Smith, Gerald Floyd; Tebbe, Anne Louise; Tinsley, Jennifer Marie; Weir, Leonard Crayton; Wikel, James Howard; Wiley, Michael Robert; Yee, Ying Kwong
PA Eli Lilly and Co., USA; Kyle, Jeffrey, Alan; et al.
SO PCT Int. Appl., 403 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D401-14
ICS C07D401-12; C07D417-14; C07D409-14; C07D405-14; C07D213-74; A61K031-395; A61K031-435; A61K031-495; A61P007-02; C07D401-14; C07D213-00; C07D213-00; C07D211-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 28, 63
FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| PI WO 2000039118 | A1 | 20000706 | WO 1999-US29946 | 19991215 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1140903 | A1 | 20011010 | EP 1999-964279 | 19991215 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| PRAI US 1998-113556P | P | 19981223 | | |
| WO 1999-US29946 | W | 19991215 | | |

OS MARPAT 133:89437
GI




I II

AB The title compds. [I; A3-A6, together with the two carbons to which they are attached, complete a substituted benzene in which A3 = CR3, A4 = CR4,

A5 = CR5, and A6 = CR6 (wherein R3 = H, Me, MeO, etc.; one of R4 and R5 = H, alkyl, halo, etc.; the other of R4 and R5 = H; R6 = H, Me, F, etc.); L1 = CONH; Q1 = 2-pyridinyl (un)substituted at the 5-position, 3-pyridinyl (un)substituted at the 6-position, 2-pyrimidinyl (un)substituted at the 5-position, etc.; R2 = L2Q2 (L2 = NHCO, NHCH2, OCH2, etc.; Q2 = (un)substituted piperidinyl, piperazinyl, Ph, etc.)] and their pharmaceutically acceptable salts, useful as inhibitors of factor **Xa** (no data), were prepd. and formulated. E.g., a multi-step synthesis of II.HCl was given. In general, compds. I are effective at 0.01-1000 mg/kg/day.

ST arom amide heteroaryl prepn formulation factor **Xa** inhibitor anticoagulant

IT Anticoagulants
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 280769-11-1P 280769-16-6P 280769-22-4P 280769-23-5P 280769-24-6P
280769-46-2P 280769-59-7P 280769-68-8P 280769-83-7P 280770-51-6P
280770-52-7P 280770-59-4P 280770-66-3P 280770-79-8P 280770-91-4P
280770-93-6P 280770-95-8P 280771-19-9P 280771-47-3P 280771-49-5P
280771-53-1P 280771-55-3P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 280768-65-2P 280768-66-3P 280768-67-4P 280768-68-5P 280768-69-6P
280768-70-9P 280768-71-0P 280768-72-1P 280768-73-2P 280768-74-3P
280768-75-4P 280768-76-5P 280768-77-6P 280768-78-7P 280768-79-8P
280768-80-1P 280768-81-2P 280768-82-3P 280768-83-4P 280768-84-5P
280768-85-6P 280768-86-7P 280768-87-8P 280768-88-9P 280768-89-0P
280768-90-3P 280768-91-4P 280768-92-5P 280768-93-6P 280768-94-7P
280768-95-8P 280768-96-9P 280768-97-0P 280768-98-1P 280768-99-2P
280769-00-8P 280769-01-9P 280769-02-0P 280769-03-1P 280769-04-2P
280769-05-3P 280769-06-4P 280769-07-5P 280769-08-6P 280769-09-7P
280769-10-0P 280769-12-2P 280769-13-3P 280769-14-4P 280769-15-5P
280769-17-7P 280769-18-8P 280769-19-9P 280769-20-2P 280769-21-3P
280769-25-7P 280769-26-8P 280769-27-9P 280769-28-0P 280769-30-4P
280769-33-7P 280769-36-0P 280769-39-3P 280769-40-6P 280769-41-7P
280769-42-8P 280769-43-9P 280769-44-0P 280769-45-1P 280769-47-3P
280769-48-4P 280769-49-5P 280769-50-8P 280769-51-9P 280769-52-0P
280769-53-1P 280769-54-2P 280769-55-3P 280769-56-4P 280769-57-5P
280769-58-6P 280769-60-0P 280769-61-1P 280769-62-2P 280769-63-3P
280769-64-4P 280769-65-5P 280769-66-6P 280769-67-7P 280769-69-9P
280769-70-2P 280769-71-3P 280769-72-4P 280769-73-5P 280769-74-6P
280769-75-7P 280769-76-8P 280769-77-9P 280769-78-0P 280769-79-1P
280769-80-4P 280769-81-5P 280769-82-6P 280769-84-8P 280769-85-9P
280769-86-0P 280769-89-3P 280769-91-7P 280769-92-8P 280769-93-9P
280769-94-0P 280769-95-1P 280769-96-2P 280769-97-3P 280769-98-4P
280769-99-5P 280770-00-5P 280770-01-6P 280770-02-7P 280770-03-8P
280770-04-9P 280770-05-0P 280770-06-1P 280770-07-2P 280770-08-3P
280770-09-4P 280770-10-7P 280770-11-8P 280770-12-9P 280770-13-0P
280770-14-1P 280770-15-2P 280770-16-3P 280770-17-4P 280770-18-5P
280770-19-6P 280770-20-9P 280770-21-0P 280770-22-1P 280770-23-2P
280770-24-3P 280770-25-4P 280770-26-5P 280770-27-6P 280770-28-7P
280770-29-8P 280770-30-1P 280770-31-2P 280770-32-3P 280770-33-4P
280770-34-5P 280770-35-6P 280770-36-7P 280770-37-8P 280770-38-9P
280770-39-0P 280770-40-3P 280770-41-4P 280770-42-5P 280770-43-6P
280770-44-7P 280770-45-8P 280770-46-9P 280770-47-0P 280770-48-1P
280770-49-2P 280770-50-5P 280770-53-8P 280770-54-9P 280770-55-0P
280770-56-1P 280770-58-3P 280770-60-7P 280770-61-8P 280770-62-9P
280770-63-0P 280770-64-1P 280770-65-2P 280770-67-4P 280770-68-5P
280770-69-6P 280770-70-9P 280770-71-0P 280770-72-1P 280770-73-2P

280770-74-3P 280770-75-4P 280770-76-5P 280770-77-6P 280770-78-7P
280770-80-1P 280770-81-2P 280770-82-3P 280770-83-4P 280770-84-5P
280770-85-6P 280770-86-7P 280770-87-8P 280770-88-9P 280770-89-0P
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280770-98-1P 280770-99-2P 280771-00-8P 280771-01-9P 280771-02-0P
280771-03-1P 280771-04-2P 280771-05-3P 280771-06-4P 280771-07-5P
280771-08-6P 280771-09-7P 280771-10-0P 280771-11-1P 280771-12-2P
280771-13-3P 280771-14-4P 280771-15-5P 280771-16-6P 280771-17-7P
280771-18-8P 280771-20-2P 280771-21-3P 280771-22-4P 280771-23-5P
280771-24-6P 280771-25-7P 280771-26-8P 280771-27-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 280771-28-0P 280771-29-1P 280771-30-4P 280771-31-5P 280771-32-6P
280771-33-7P 280771-34-8P 280771-35-9P 280771-36-0P 280771-37-1P
280771-38-2P 280771-39-3P 280771-40-6P 280771-41-7P 280771-42-8P
280771-43-9P 280771-44-0P 280771-45-1P 280771-46-2P 280771-48-4P
280771-50-8P 280771-51-9P 280771-52-0P 280771-54-2P 280771-56-4P
280771-57-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT **9002-05-5**, Factor **Xa**
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); **BIOL (Biological study)**
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 67-64-1, Acetone, reactions 75-64-9, tert-Butylamine, reactions
78-84-2, Isobutyraldehyde 78-93-3, Methylethyl ketone, reactions
89-98-5, 2-Chlorobenzaldehyde 96-22-0, 3-Pentanone 96-33-3 97-96-1,
2-Ethylbutyraldehyde 98-01-1, Furan-2-carboxaldehyde, reactions
98-74-8, 4-Nitrobenzenesulfonyl chloride 98-80-6, Phenylboronic acid
99-88-7, 4-Isopropylaniline 99-92-3 100-52-7, Benzaldehyde, reactions
104-88-1, 4-Chlorobenzaldehyde, reactions 105-36-2, Ethyl bromoacetate
105-58-8, Diethyl carbonate 106-47-8, 4-Chloroaniline, reactions
107-13-1, 2-Propenenitrile, reactions 108-94-1, Cyclohexanone, reactions
110-52-1, 1,4-Dibromobutane 111-42-2, reactions 120-92-3,
Cyclopentanone 122-85-0, 4-Acetamidobenzaldehyde 123-11-5,
4-Methoxybenzaldehyde, reactions 123-19-3, 4-Heptanone 123-38-6,
Propionaldehyde, reactions 123-75-1, Pyrrolidine, reactions 134-20-3
141-75-3, Butyryl chloride 177-11-7, 1,4-Dioxa-8-azaspiro[4.5]decane
320-98-9, 5-Fluoro-2-nitrobenzoic acid 446-10-6, 4-Fluoro-2-nitrotoluene
500-22-1, Pyridine-3-carboxaldehyde 502-42-1, Cycloheptanone 503-29-7,
Azetidine 583-60-8, 2-Methylcyclohexanone 583-68-6,
2-Bromo-4-methylaniline 585-71-7, (1-Bromoethyl)benzene 587-04-2,
3-Chlorobenzaldehyde 589-16-2, 4-Ethylaniline 610-14-0, 2-Nitrobenzoyl
chloride 620-23-5 701-57-5, Methyl 4-nitrophenyl sulfide 765-43-5,
Cyclopropylmethylketone 769-10-8, 2-Fluoro-6-nitrotoluene 872-85-5,
4-Pyridinecarboxaldehyde 873-38-1, 2-Bromo-4-chloroaniline 1003-04-9,
Tetrahydrothiophen-3-one 1003-98-1, 2-Bromo-4-fluoroaniline 1008-91-9,
1-(4-Pyridyl)piperazine 1072-72-6, Tetrahydrothiopyran-4-one
1072-98-6, 2-Amino-5-chloropyridine 1120-72-5, 2-Methylcyclopentanone
1121-60-4, Pyridine-2-carboxaldehyde 1122-54-9, 4-Acetylpyridine
1126-09-6, Ethyl isonipecotate 1489-69-6, Cyclopropanecarboxaldehyde
1603-41-4, 2-Amino-5-methylpyridine 1710-98-1, 4-tert-Butylbenzoyl
chloride 1776-53-0, 4-Aminocyclohexanecarboxylic acid 1793-07-3,
2-Carbomethoxyphenyl isocyanate 1882-69-5, 5-Methoxy-2-nitrobenzoic acid
2148-56-3, 2-Amino-6-chlorobenzoic acid 2366-70-3, 4,4,4-Trifluorobutan-
2-one 2516-95-2, 5-Chloro-2-nitrobenzoic acid 3113-72-2,

5-Methyl-2-nitrobenzoic acid 3678-63-5, 4-Chloro-2-picoline 4315-09-7, 4-Nitroisophthalic acid 4363-93-3, Quinoline-4-carboxaldehyde 4771-47-5, 3-Chloro-2-nitrobenzoic acid 4786-20-3, 2-Butenenitrile 4897-84-1, Methyl 4-bromobutyrate 4920-80-3, 3-Methoxy-2-nitrobenzoic acid 5350-93-6 5372-81-6, 2-Aminoterephthalic acid dimethyl ester 5428-89-7, 2-Amino-5-chloropyrimidine 5437-38-7, 3-Methyl-2-nitrobenzoic acid 5469-69-2, 3-Amino-6-chloropyridazine 5470-22-4, 4-Chloropicolinic acid 5538-51-2, **Acetylsalicylic acid** chloride 6280-88-2, 4-Chloro-2-nitrobenzoic acid 7304-32-7, 2-Fluoro-5-nitrobenzoic acid 7379-35-3, 4-Chloropyridine hydrochloride 7486-35-3, Tributyl(vinyl)tin 10177-29-4, 4-Chloronicotinic acid 10200-59-6, Thiazole-2-carboxaldehyde 14002-51-8, 4-Biphenylcarbonyl chloride 17012-21-4, Methyl 1-benzylpyrrolidine-3-carboxylate 19235-89-3, 4-Chloro-2-cyanopyridine 19524-06-2 21717-96-4, 2-Amino-5-fluoropyridine 29943-42-8, Tetrahydro-4H-pyran-4-one 40499-83-0, 3-Hydroxypyrrolidine 55737-66-1, 4-Methoxycarbonyl-2-nitrobenzoic acid 57260-71-6, N-tert-Butoxycarbonylpiperazine 57946-63-1, 2-Bromo-4-trifluoromethylaniline 76143-33-4, 5-Methoxycarbonyl-2-nitrobenzoic acid 79099-07-3, 1-tert-Butoxycarbonyl-4-piperidone 84358-13-4, 1-tert-Butoxycarbonyl-isonipecotic acid 93913-86-1 103057-44-9, 1-tert-Butoxycarbonyl-3-hydroxypyrrolidine 109384-19-2, 1-tert-Butoxycarbonyl-4-hydroxypiperidine 118486-94-5, 2-(Tributylstannyl)furan 124252-41-1, 4-(Tributylstannyl)pyridine 141699-55-0, 1-tert-Butoxycarbonyl-3-hydroxyazetidine 173382-28-0 175278-17-8 183158-31-8 186550-13-0 218777-23-2 219493-02-4 280115-99-3 280769-38-2 280774-10-9 280774-11-0 280774-12-1 280774-13-2

RL: RCT (Reactant); RACT (Reactant or reagent)
(prepn. of heteroaryl-substituted arom. amides as factor **Xa** inhibitors)

IT 385-02-4P 394-01-4P 1709-59-7P 2965-22-2P 2976-30-9P 3356-88-5P 5470-49-5P 5731-17-9P 17459-03-9P 18229-61-3P 33890-03-8P, 4-Aminoisophthalic acid 61014-96-8P 63069-48-7P, 4-Chloro-2-iodoaniline 70684-84-3P 75541-82-1P 76842-15-4P 97776-06-2P 116721-57-4P 117145-55-8P 117145-66-1P 123855-51-6P, 1-tert-Butoxycarbonyl-4-hydroxymethylpiperidine 130234-74-1P 130309-46-5P 130658-67-2P 137076-22-3P, 1-tert-Butoxycarbonyl-piperidine-4-carboxaldehyde 138647-49-1P 142374-19-4P 154348-17-1P 159974-55-7P 159974-59-1P 166954-15-0P 168077-29-0P 183170-69-6P 184368-74-9P 188604-84-4P 202202-36-6P 217487-18-8P 219492-85-0P 229342-58-9P 229342-63-6P 229343-30-0P 251548-94-4P 280771-58-6P 280771-59-7P 280771-60-0P 280771-61-1P 280771-62-2P 280771-63-3P 280771-64-4P 280771-65-5P 280771-66-6P 280771-67-7P 280771-68-8P 280771-69-9P 280771-70-2P 280771-72-4P 280771-73-5P 280771-75-7P 280771-78-0P 280771-79-1P 280771-80-4P 280771-81-5P 280771-82-6P 280771-83-7P 280771-84-8P 280771-85-9P 280771-87-1P 280771-88-2P 280771-90-6P 280771-91-7P 280771-93-9P 280771-94-0P 280771-96-2P 280771-97-3P 280771-98-4P 280771-99-5P 280772-00-1P 280772-01-2P 280772-02-3P 280772-03-4P 280772-05-6P 280772-07-8P 280772-09-0P 280772-10-3P 280772-11-4P 280772-13-6P 280772-14-7P 280772-15-8P 280772-17-0P 280772-18-1P 280772-19-2P 280772-20-5P 280772-21-6P 280772-22-7P 280772-23-8P 280772-24-9P 280772-25-0P 280772-26-1P 280772-27-2P 280772-28-3P 280772-29-4P 280772-31-8P 280772-32-9P 280772-34-1P 280772-35-2P 280772-36-3P 280772-37-4P 280772-38-5P 280772-39-6P 280772-40-9P 280772-41-0P 280772-42-1P 280772-43-2P 280772-44-3P 280772-45-4P 280772-47-6P 280772-48-7P 280772-49-8P 280772-50-1P 280772-51-2P 280772-53-4P 280772-54-5P 280772-55-6P 280772-56-7P 280772-57-8P 280772-59-0P 280772-60-3P 280772-61-4P 280772-62-5P 280772-63-6P 280772-65-8P 280772-66-9P 280772-67-0P 280772-68-1P 280772-69-2P 280772-71-6P 280772-72-7P 280772-74-9P 280772-75-0P 280772-77-2P 280772-78-3P 280772-79-4P 280772-80-7P 280772-82-9P 280772-83-0P 280772-84-1P 280772-85-2P 280772-87-4P 280772-88-5P 280772-89-6P 280772-90-9P 280772-92-1P 280772-93-2P